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VITAMINS AND THE EAR, NOSE AND THROAT.

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It is true that as yet we have very little definite information about this subject; but it is equally true that we already realize its great importance, in our daily practice. We know that the vitamins undoubtedly play a very real part in the health and disease of the ear, nose and throat. In no other field of research have there been greater recent advances than in knowledge of the vitamins, and the part they play — in plant, animal and human life. In fact, it now appears definitely established that these substances, only so recently discovered, are essential to life itself. The tissues of the ectoderm, mesoderm and endoderm all demand vitamins. Consequently, in service to our patients, it is of immediate importance for us to learn all that we possibly can of the effects of vitamin deficiencies on the tissues and organs derived from these three germ layers in the ear, nose and throat.

The objects of THE LARYNGOSCOPE in presenting this subject are: (1) To state the problem of the vitamins and the ear, nose and throat, and to put on record where the subject stands today; and (2) To present to otolaryngologists a brief resumé of the general literature on the subject of the vitamins.

Out of the bewildering mass of information, not yet digested or applied, would it be possible to deduce some facts on which we can already rely? If so, in the study of the "Vitamin Alphabet", such facts would be of immediate value — particularly to those of us who are just learning our "A, B, C's."

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1. Although there is no specific action of any one vitamin for one particular type of structure, yet it is already established that certain vitamins have an especial effect on certain structures. It is therefore of immediate interest to consider what structures in the ear, nose and throat are derived from the three embryonic germ layers. In the internal ear, all of the epithelial structures in both the cochlear and vestibular portions, as well as the nervous tissues, are derived from the ectoderm. The supporting tissues of the membranous labyrinth, and the bony otic capsule, come from the mesoderm. In the middle ear, the epithelium is derived from the first pair of pharyngeal pouches — and is therefore from the endoderm. The bone of the ossicles is from the mesoderm, and their epithelial covering from the endoderm. In the tympanum, the bone, muscles and supporting tissues are from the mesoderm; and the lining epithelium from the endoderm. In the eustachian tube, the cartilage and bone are from the mesoderm and the epithelial lining from the endoderm.

In the nose, the olfactory epithelium and the mucous glands are from the ectoderm; the cavernous structures of the turbinates and all supporting tissue — from the mesoderm.

In the mouth, the lining epithelium is from the ectoderm; the muscles and bones from the mesoderm; the taste buds from both the ectoderm and endoderm; the tonsils and adenoids from the mesoderm. In the teeth, the enamel is from the ectoderm; the dentine and cementum from the mesoderm. The alveolar processes are from the mesoderm. The salivary glands, from the ectoderm.

While it is naturally impossible to draw any hard and fast lines in prescribing vitamins for abnormal conditions in these various structures, nevertheless it is already apparent that each vitamin has a preponderant effect on special structures. We know that keratinization of the cornea responds to "A"; in fact, it seems established that "A" is peculiarly concerned with the disease and health of epithelial tissues, particularly those epithelial structures that are derived from the ectoderm. "A" is also concerned with epithelial structures in the nasopharynx, eustachian tube and middle ear — which are derived from the endoderm. "B" is actually termed the "antineuritic vitamin" and it has a particular relation to

nervous tissues — which are derived from the ectoderm. "C" appears to be directly related to tissues derived from the mesoderm — particularly the connective tissue and blood capillaries. The swollen, bleeding gums of scurvy immediately call for "C" therapy. "D" is unquestionably related to bony structures — derived from the mesoderm. The simplest example is that an absence of "D" causes rarefaction of the alveoli and that "D" therapy, providing other factors are normal, can have a direct restorative effect on these structures.

2. We already are sure that no vitamin can be expected to improve any condition that has not been caused by a lack of the same vitamin. One might coin a slogan — "No deficiency — no cure." For example, if a lesion of the internal ear or VIII Nerve has been caused by syphilis, quinine or a neuroma, it would be an idle gesture to prescribe vitamins.

3. On the contrary, we also know that the proper ingestion of vitamins will prevent many pathologic states in the ear, nose and throat, as elsewhere in the body; and furthermore that if we can be sure of an existing deficiency, practically all such conditions can be cured.

4. Under any circumstances, even if the lesion is due to a vitamin deficiency, it seems clear that we cannot expect any vitamin to regenerate the VIII Nerve itself, unless the peripheral structures are viable. Animal experiments have shown that a peripheral sensory nerve degenerates, beginning at its peripheral portion and extending inward, up to its ganglion cells. Regeneration of this nerve cannot occur if the ganglion cells themselves have been destroyed. If, however, the ganglion cells are still viable, a regeneration has been demonstrated, beginning at the spinal cord and extending toward the periphery — at the rate of about 1 mm. a day.[1]

In applying this concept to the ear, it would seem that we cannot expect a return of function of the VIII Nerve itself without considering certain facts. The ganglion cells of the cochlear nerve are represented by spiral ganglia which occur in groups in the internal ear itself. Distal to these are the dendritic fibers of the ganglion cells which end on the hair cells; proximally, the fibers extend to the first synapse in

the medulla. Similarly the vestibular ganglion cells are contained in Scarpa's ganglion. The proximal axonic fibers of these cells also end in the medulla. Therefore, if we are looking for an improvement in the function of the internal ear, it would seem necessary to postulate the following: (1) The impaired function must be directly due to a lack of vitamins, and (2) The cells of Scarpa's ganglion and of the spiral ganglia must still be viable. If these ganglia are destroyed, no regeneration can be expected. If however, a degeneration has been produced by a vitamin deficiency, and the Scarpa's and the spiral ganglia are not yet destroyed, it seems reasonable to expect that regeneration can occur within the internal ear itself, just as regeneration has been proved to occur in peripheral nerve filaments in other parts of the body.

5. We also realize that it is a simple matter to demonstrate a deficiency in "A" — if the patient has xerophthalmia; a deficiency in "B" — if the patient exhibits beriberi; and a deficiency in "C" — if the patient obviously has scurvy. Such advanced states, however, are so rare that probably none of us will ever see more than one or two of them. The difficulty lies in the much larger number of patients who have only a moderate deficiency; and in the still larger number who have only a mild deficiency, we are even more at a loss to make a diagnosis of a lack of one or more vitamins. The entire matter would be one of the greatest simplicity — if only we had simple and accurate methods of discovering a moderate or mild deficiency for each of the vitamins. To be sure, certain laboratory tests are already available; for example, the exact amount of pyruvic acid in the blood and the urine can be determined, and this gives an index of the lack of "B_1". If the amount of pyruvic acid in the blood is above the normal level, "B_1" therapy is indicated. As to "C", (ascorbic acid), it can actually be detected in the urine and in the blood plasma. If the ascorbic acid in the blood plasma is below the normal level, then vitamin C therapy is indicated. It already appears probable that more and more laboratory tests will soon be available. However, it must be realized that only a few clinical laboratories are equipped to make the present tests; and in many parts of the country such services are not available to the clinician. Under all circumstances, the best method that we have at the present time is to make careful inquiry into the diet of the patient.

For years, this has been emphasized by Shurly,[2, 3] E. R. Lewis,[4] and Moose.[5]

6. The natural source of vitamins to be given to our patients is in the foodstuffs they consume. It is also important to recognize that this is the less expensive form of vitamin therapy. However, in what we see in print and in what we hear over the radio, we realize that the advertising claims of such sales-talk are not to be relied upon either as to quality or quantity. In addition, the studies of the vitamins have made it clear that one of the real penalties of our civilization is that we are afflicted with "refined" foods. Ironically, many of these foods which have been artificially deprived of the very vitamins we need, are advertised as "Health Foods." At the present time, the only way in which we can regulate the dosage is to prescribe the vitamins themselves; even then we must be careful to rely upon trustworthy pharmaceutical houses.

7. However, in any vitamin deficiency, we should not limit our treatment to the direct administration of a vitamin itself. It is generally recognized that a deficiency in just one vitamin rarely, if ever, exists. Therefore, we should supplement a vitamin with foods which provide an abundance, not only of any one vitamin, but of others as well. We must always bear in mind that almost every food in its natural state contains several vitamins.

8. In our dilemma, we derive comfort from realizing that a vitamin is not a *drug*. Therefore at present we do not need to be unduly anxious if we prescribe a somewhat larger amount of vitamins than the patient needs — with the exception of "D". For example, it seems well established that "B_1" — (thiamin chloride), is stored in the body in very small amounts. It is water soluble, and its excess is excreted in the urine and feces. If, therefore, the patient takes $4.50 worth of "$B_1$" and retains 50c worth of it — the only damage done is to his pocketbook — *i.e.*, $4.00 worth is promptly eliminated by the kidneys and bowels.

9. We already know that individuals exhibit a great difference in their vitamin requirements. We cannot lay down any mathematical rule as to dosage. Some people may not be

able to absorb vitamins properly; and others who can absorb them, cannot properly retain and utilize them.

10. There are other complicating factors as to dosage. We must ever keep in mind that many conditions increase the need for vitamins. For example, if a patient is taking iron. because of anemia; or is taking thyroid, whether because of a thyroid deficiency or in order to reduce weight — the vitamin requirements may be markedly increased. Both iron and thyroid actually oxidize vitamins, and consequently make it necessary to ingest larger amounts of them. Similarly, exercise increases the need for vitamins. Alcohol is not only a stimulant, but supplies a definite number of calories to the body. It naturally contains no vitamins whatever. Therefore, anyone who takes an appreciable amount of alcohol, requires more vitamins than he would otherwise need; and the chronic alcoholic may exhibit a desperate need for a large intake of vitamins. Nature itself has provided foods rich in minerals and vitamins — and adequate in calories. In the refining of these foods for human consumption, vitamins have been lost. Thus the caloric intake of an individual is usually adequate, but the vitamin intake is not.

11. Just as throughout the body, the defense mechanism of all ear, nose and throat tissues requires the presence of an adequate amount of all vitamins. If, therefore, we bear this in mind, we may look forward to the day when many pathologic conditions of the ear, nose and throat which we are observing in our daily practice, will respond favorably to appropriate vitamin therapy.

12. If we consider that a patient does have a vitamin deficiency, we should not only prescribe generous amounts, but should continue the administration of the vitamins over a long period of time. It is true that ulcerations of the oral mucosa in cases of pellagra have shown a marked improvement only twelve hours after the administration of nicotinic acid. Similar "immediate cures" have occurred. On the average, however, we should continue vitamin therapy over an appreciable period of time before concluding that we can expect no benefit.

Up to this time, very few otolaryngologists have made a definite study of this subject. Hundreds, and perhaps thou-

sands, are prescribing vitamins, in a necessarily haphazard way. Several otolaryngologists, notably Veasey[6] and Brandenburg,[7] are making observations on the effect of vitamins — but as yet with indeterminate results. Those who have made the most important contributions are: Selfridge, Covell, Loch and Guggenheim.

Previously a pioneer in the rôle of the endocrines, and again in the rôle of allergy in otolaryngology, Grant Selfridge[8, 9, 10, 11, 12] has again led the field in this study of the vitamins. For the past five years, he has studied the effect of many vitamins on ear, nose and throat conditions in the human being — particularly the effect of the factors of the vitamin B Complex upon impaired hearing. Although Selfridge emphasizes that slight improvement of hearing, as shown by repeated audiograms is not to be relied upon as conclusive evidence, yet he was the first to show that it is possible for vitamins to improve the hearing.

Just as Selfridge was the first to make clinical studies of the vitamins and the ear, nose and throat, so Walter P. Covell[13, 14] was the first to make precise histopathologic studies. In an article in this issue of THE LARYNGOSCOPE, Covell presents an outline of his results to date on tissues of the middle ear, on the bony capsule of the internal ear, and on the nervous mechanism of the internal ear. He presents the results of experimental nutritional deficiencies for vitamins of the "B" group, and also for vitamins A, C, D and E. His findings are here summarized:

1. Histopathologic changes in the peripheral auditory mechanism can be readily demonstrated in animals under experimental conditions. It is not a simple matter to establish a relationship between diet and hearing for the human; and the problem must remain unsettled until such time as sufficient evidence is available. A brief summary of the most important findings for 112 animals whose diets lacked in one or the other of vitamins is presented.

2. Middle ear infection occurred more frequently for deficient rats than for those receiving a diet adequate in all nutritional factors. For avitaminoses of the "B" group, "D" and "E", the inflammatory reaction and the changes in the lining of the middle ear cavity were of a nonspecific nature.

For avitaminoses A and C the reaction on the part of the mucous membrane and submucosa, while different for each factor was, in addition, specific for each deficiency. Atrophic changes in the muscles of the middle ear occurred in "E" deficient animals and to a lesser degree in certain of the "B" group. The tensor tympani muscle revealed more extensive changes than did the stapedius muscle.

3. Increase in thickness of the periosteal layer of the otic capsule was more in evidence in "A" than in "E" deficient animals. Avitaminosis D resulted in the formation of osteoid, about the small vessels in the ossicular chain and in the otic capsule.

4. Hemorrhage into the scala tympani occurred in "B_2" deficiency; and about the nerve in its course through the modiolus, in "E" deficient animals. In "C" deficient guinea pigs, the cells of the organ of Corti were swollen and appeared to have retained fluids. The external hair cells revealed slight to moderate degenerative changes, in animals on diets lacking in "B_2".

5. Degeneration of the medullary sheath of the extreme peripheral portions of the cochlear nerve was found in almost all of the deficiencies. The extent of damage appeared to be directly related to the extent of the dietary depletion. It was, however, more marked in animals on diets which lacked "B_6", or "B_1" or "B_2". The reaction was found to be reversible, providing the missing factor had been supplied in the diet for a sufficient period of time.

Loch[15] reported on pathologic changes in the temporal bones of 56 rats and guinea pigs, deprived of different vitamins. His observations were chiefly concerned with the different layers of the otic capsule. Lack of "A" resulted in new bone formation in the periosteal layer. Lack of "E" caused areas of localized new bone; and in one instance an exostosis in Rosenthal's canal. In "C" deficiency, the endosteal and endochondral layers remained unchanged, while the contents of the medullary spaces of the periosteal layer changed from a cellular marrow to a fatty marrow. Animals lacking "D" in their diets showed a deposit of osteoid, in the periosteal and endochondral layers of the capsule.

For years, Guggenheim[16, 17, 18] has emphasized that otosclerosis is a localized entity and not a local manifestation of

a systemic disease, such as Paget's disease or osteodystrophia fibrosa of von Recklinghausen. He considers, as does the writer, that the regression theory thus far is the most logical explanation. Otosclerosis is hereditary; it has a selective effect upon certain parts of the ear — which parts are in the recently developed portion, namely the cochlea, and the round and oval window regions; dystrophic bone tends to close the oval and round windows and to obliterate the cochlea — all seemingly in an effort on the part of nature to do away with the structures whose evolution is comparatively recent. Obliteration of the fissula ante fenestram is also a sign of regression, as this structure is also absent in early organisms. In otosclerosis there is not only new bone formation but varying degrees of degeneration of the VIII Nerve; what relationship this degeneration has to the bone pathology, we do not know. Guggenheim believes the dystrophic bone is permitted to increase because of the resorption of calcium and phosphorus from the normal capsule around the otosclerotic focus. At the Children's Hospital, under a grant of the Research Study Club of Los Angeles, Guggenheim, Lewis Gunther, Victor Goodhill and Mary Irvine conducted experiments on Wistar stock white rats. The administration of vitamin D in toxic doses, ammonium chloride and parathormone, produced a resorption of calcium and phosphorus in the bony capsule of the internal ear. With proper controls for all experiments, an optimum diet — with adequate amount of phosphorus, calcium and vitamins — restored the capsule of the ear to normal — thus proving that in the rat at least reversal of this process is a fact. In the clinical application of Guggenheim's theory, patients were treated over a three-year period with dietary regulation, calcium, phosphorus and vitamins. He found that no patients under treatment showed any further deterioration of hearing, and that some showed actual improvement, even up to 30 and 40 decibels. The improvement in hearing was attributed, not to bony changes, but to the improvement in the neuropathy from B Complex therapy.

SUMMARY.

Facts already available — for use in clinical practice:

1. Each vitamin has a preponderant effect on the special structures derived from the ectoderm, mesoderm and endoderm.

2. No deficiency — no cure.

3. On the contrary, unless the tissues are actually destroyed, a deficiency state can be cured.

4. We cannot expect to improve the hearing by regeneration of the VIII Nerve unless the sensory apparatus in the internal ear is viable.

5. Advanced deficiency states are readily diagnosed. Moderate or mild states — more difficult; in these, in addition to a limited number of laboratory tests, we must rely on a careful study of the diet of the patient.

6. At present, the only way in which we can regulate the dosage is to prescribe the vitamins themselves.

7. However, we should not limit our treatment to vitamin therapy; but supplement it with foods which provide an abundance not only of any one vitamin but of others as well.

8. A vitamin is not a drug.

9. Individuals differ in their vitamin needs.

10. Complicating factors as to dosage — drugs like iron; thyroid; exercise; and alcohol. The caloric intake of an individual is usually adequate, but the vitamin intake is not.

11. The defense mechanism of all tissues requires the presence of an adequate amount of vitamins.

12. On the average, we should continue appropriate vitamin therapy over an appreciable period of time.

REVIEW OF THE LITERATURE ON THE GENERAL SUBJECT OF THE VITAMINS.

When we realize that a very large part of all recent medical literature is on the subject of the vitamins, it is apparent that even short abstracts of the available literature would require an entire book — and a very large one at that. For this purpose, therefore, it is necessary to refer to only a few of the recent contributions. In addition it is not possible to classify the reviews precisely under the headings of the different vitamins themselves — because many authors discuss one or more of the vitamins. However, in general, we will study them in the order of A, B, C, D, E, and K.

McLester[19] states that in no other field of medical knowledge has there been recorded such a far-reaching advance as has been made during the past two decades in the field of nutrition. Fighting the way to the development of a healthier, more vigorous race, this advance marks an epoch in man's progress.

Fishbein[20] agrees that the achievements in the science of nutrition are among the most significant of all that have been made in the entire field of modern medical science. The original five letter alphabet for the vitamins has been extended; and even the original letters have begun to be subdivided. Vitamin B, instead of being just one or two vitamins, may actually include eight or more specific factors or principles. "B_1" (thiamin) — allowable claims: (1) Of value in correcting and preventing beriberi; (2) Of value in correcting and preventing anorexia of dietary origin, in certain cases; (3) Of value in securing the optimal growth of infants and children; (4) The daily requirement appears to be not less than 50 units for the infant and 200 units for the adult; (5) It appears that there is an increased requirement for thiamin during greatly augmented metabolism — as in febrile conditions, hyperthyroidism, or vigorous muscular activity. Nicotinic acid. Allowable claim: Specific in the treatment of acute pellagra in relapse. The protective dose, and the amount which should be present in a well-balanced ration, are unknown.

VITAMIN A.

Bessey and Wolbach,[21] Clausen,[22] Munsell[23] and Booher[24] discuss vitamin A, from every angle. In a vitamin A deficiency, the pathologic features are the consequence of epithelial changes. Lesions of the nervous system in human beings, with vitamin A deficiency, have not been reported. Such changes, however, have been found in animals; in fact, Edward Mellanby[25] speculates that the epithelial changes are secondary to loss of neurotrophic control. However, an impressive number of workers fail to observe signs of nerve lesions. Severe degeneration of muscle is common in man, guinea pigs and rats. Night blindness is an early symptom of deficiency of vitamin A.

Zimmerman, Cowgill and Fox[26] state that vitamin A deficiency produces a degeneration of the medullary sheaths of peripheral nerves and of the ascending tracts of the spinal cord, chiefly the spino-cerebellar tracts.

Morch[27] classifies the symptoms of an "A" deficiency:

Subjective:

1. Irritation and secretion — conjunctiva.

2. Sensation of dryness in pharynx and rhinopharynx, with irritation in larynx.

3. Depraved taste.

4. Absence or diminution of sense of smell.

5. Periodic crises of thirst.

6. Lassitude and listlessness.

7. Need of long periods of sleep.

8. Lumbago and myalgias.

Objective:

1. Conjunctival signs.

2. Dry appearance of pharynx with glossy mucus.

3. Dryness with sticky secretion — rhinopharynx.

4. Dryness with sticky secretion — interarytenoid space.

5. Scales and crusts — vestibule of nose.

6. Scales and crusts — external auditory canal.

7. Rhagades in the region of the labial commissures.

Administration of excessive doses of Vitamin A.

1. Burning sensation of eyes but no conjunctival secretion.

2. Urinary frequency.

3. Formation of bump at site of injection (buttocks).

4. Eruption over limbs and trunk.

5. Agitation and depression.

6. Somnolence and lassitude.

Wolbach and Bessey[28] have found that growth of bone ceases in vitamin A deficiency; and probably the growth of the central nervous system continues after the growth of the skeleton has ceased. This period of unequal growth between the two systems occurred in animals of forty to sixty days of age. Rats became paralyzed on the fiftieth day. No readily discernible changes in the central nervous system or spinal ganglia are to be found other than those explainable through mechanical factors due to differences in growth between nervous tissue and bone.

Wilder and Rutledge[29] state that concentrates of "A" are available principally in the form of fish liver oils. Carotene is also available. The therapeutic dose, in the neighborhood of 10,000 units daily. As yet a satisfactory preparation which can be administered by injection is not available. Carotene, cod liver oil and concentrates of "A" have been given intramuscularly but their widespread clinical use is not practical. There is little fear of any toxic effect from "A".

Mellanby[30] described bony changes in the temporal bones of animals on a diet lacking in vitamin A. Of chief interest was the formation of an exostosis in the wall of the internal auditory canal. He successfully demonstrated that new bone formation due to this deficiency could result in atrophic changes in the VIII Nerve, by pressure.

THE VITAMIN B COMPLEX.

The up-to-the-minute classification of the factors of the B Complex is as follows: B_1, which is thiamin chloride;

B_2 complex, which consists of B_2, (now regarded as riboflavin); nicotinic acid; B_6; and the filtrate factor, which is again divided into pantothenic acid, and the Morgan anti-gray hair factor.

Nelson[31] reminds us that "B_1" — the anti-beriberi vitamin — prevents beriberi in man and polyneuritis in animals. He also states that riboflavin is necessary for growth in chicks and rats, and for the prevention of cataract in rats; and that nicotinic acid is effective in the prevention of human pellagra.

Williams:[32] The function of "B_1" is probably not merely to get rid of pyruvic acid, but to utilize it in some metabolic process. The diagnostic value of "B_1" therapy is largely lost if crude natural preparations are used — because of the uncertainty of their standardization; and of the presence of other vitamins which may be responsible for the observed effects. However, in the long run, we must look to the grocery store rather than to the drug store for a normal intake.

Cowgill[33] emphasizes that the capacity to store "B_1" is limited. In the pigeon, the rat and the dog, the time required for a shortage of "B_1" to become evident, varies from about 10 days to 3 or 4 weeks. This limited capacity for storage is obviously of great importance in clinical practice. In "B_1" deficiency, the rotational movements exhibited by animals suggest lesions in the vestibular nuclei; perivascular hemorrhages in the brain-stem have been noted. "B_1" exerts a demonstrable action only in the "B_1" deficient animal. No toxic symptoms of any kind are observed when doses approximating 25,000 or more times the estimated daily requirement are administered; so it is evident that this dietary essential now available in pure form for its clinical use is not to be regarded as a drug. Instead it is to be considered a normal and necessary part of the organism, which exerts its function whenever it is needed. Any excessive supply beyond a moderate amount capable of storage in the tissues for a relatively short period, is eliminated through the kidneys. "B_1" is readily absorbed, whether given by mouth or parenterally.

Wright and Baker[34] state that the daily excretion of "B_1" in the urine, by a healthy human on a good mixed diet, varies between 40 and 180 units — most frequently between 60 and 80 units. One week on a low "B_1" diet reduces this amount to about 13 units.

Vedder:[35] Beriberi is directly caused by deficiency of "B_1" — and possibly other deficiencies in the diet. Degenerative changes in the nervous system include: — a multiple peripheral neuritis; degeneration of the medullary sheath; and in some cases, fragmentation of the axis cylinder. In most cases these degenerative changes are not to be regarded as complete, which would mean the death of the cell — from which there could be no recovery; but they do indicate a very complete exhaustion of the affected parts. Degeneration of the myelin sheath is constant; the myelin is broken up into balls or beads and eventually disappears. When this occurs, the axis cylinders may show a coiled appearance and in certain cases are fragmented or atrophied. However, the majority of the nerve cylinders appear normal, even when the medullary sheath shows advanced degeneration.

Strauss:[1] "B_1" deficiency in man involves predominantly the nervous and circulatory systems. Such clinical descriptions under the name beriberi, date back to ancient Chinese medical writings. During the past decade, it has been shown that beriberi has been endemic in the United States — although instead of being recognized as a "B_1" deficiency in the Western World, it has been termed alcoholic polyneuritis, the toxic polyneuritis of pregnancy, diabetic, biliary and gastrogenous polyneuritides, postinfectious polyneuritis, the Korsakoff syndrome — and other similarly indefinite and misleading names. These polyneuritides differ only in the mechanism by which the "B_1" deficiency is brought about. For example, the chronic alcoholic usually ingests a sufficient amount of "B_1", but the alcohol increases the total "B_1" requirement. The pregnant woman, when nauseated, often restricts her diet to concentrated carbohydrate foods, low in "B_1" content; further, the "B_1" requirement is increased by gestation. It is quite possible that some of the supposed symptoms of "B_1" deficiency are in reality due to some other factor — such as deficiency of riboflavin and nicotinic acid. "B_1" was isolated only recently and it is as yet too early to know the effects of pure "B_1". An absence in the diet of "B_1" for about 20 days may be required for the appearance of the first symptoms. Should no treatment be instituted, the end stages may be reached within a matter of weeks. Peripheral nerves are capable of regeneration as long as the cell body in the spinal cord or posterior ganglion remains viable. Since this regeneration commences at the cell body and progresses

distally at a rate of about 1 mm. a day, it is apparent that months will be required for the complete repair of advanced degeneration. Therefore, treatment must continue unremittingly until regeneration occurs.

Food sources of "B_1" are presented by Munsell:[36] It is present in a wide variety of foods, but there are few foods of plant or of animal origin that may be considered potent sources of this factor. In planning an adequate diet, it is necessary to depend on several food items to furnish the day's supply of "B_1". This is in direct contrast to vitamin A and vitamin C, in which a single food may furnish the major portion of the requirement for the day. The problem of planning for "B_1" is further complicated in that it is desirable to insure an adequate supply each day — since "B_1" is not stored in the body to any great extent. Vegetables, including potatoes, may be regarded as forming one of the more important groups to be depended on. Exclusive of legumes, they may be considered on a par with one another, since they do not show differences among themselves that make it feasible to group them for their "B" content on the basis of any particular physical characteristic — such as color for instance. Although fruits may be rated as only fair sources, they are important in that they are generally eaten raw and in relatively large quantities, if used at all. "B_1" tends to be concentrated in the germ portion and outer or bran layer of seeds. Legumes, nuts and whole grains are among the good food sources. Refined cereals and flours, however, contain very little "B_1" — because the germ and the bran layer are largely removed during the refining process. Eggs, muscle meats and, more especially, the organ meats are rated as good sources. Milk becomes an important source of "B_1", when considered on the basis of the quantity usually consumed, and that it may be used without treatment, which would tend to lessen its potency. In other words, it is taken raw. "B_1" is inactivated by heat in the presence of moisture. However, this may not be considered significant up to one hour's cooking at 100° C. Losses in food under conditions comparable to those in baking may be as high as 50 per cent. Although "B_1" is not readily destroyed at the temperature of boiling water, the greatest loss may take place in foods that are boiled. "B_1" is soluble in water, and it is easily conceivable that a large proportion of the vitamin may go into solution in the cooking water and be lost. Unless this liquid is served in some other

way to the person eating the food, the food itself should be held a questionable source of "B_1", even though in the untreated form it is rated as a good source. The inclusion of a food item in the diet is not what is important — it is its actual nutritive value when consumed. Unfortunately, fruits, meats, milk and eggs, which constitute good sources, are among the high cost foods and they are the first to be omitted in the low cost diet.

In the elaborate book, "Vitamin B_1", Williams and Spies[37] make a sweeping statement that animals of all species deprived of "B_1" over a period of time, develop neural degeneration.

Zimmerman and Burack[38] found that dogs in which the chronic deficiency state developed, showed demyelinization of the peripheral nerves and minimal lesions in the columns of Goll.

Becker[39] discusses the B Complex: In 1913, McCollum and his co-workers demonstrated the "water-soluble" vitamins and suggested that this new vitamin was identical with the anti-beriberi substance. In 1926, Smith and Hendrick established the dual nature of this water-soluble vitamin. They employed yeast or yeast extracts which had been heated sufficiently to destroy the antineuritic vitamin, and found these substances effective in restoring growth in rats. Thus they demonstrated in yeast the existence of a heat-stable factor distinct from the antineuritic substance. A dozen or more names have been employed to designate the substance which prevents or cures polyneuritis. The term generally agreed upon is thiamin. or "B_1". In 1926, Jansen and Donath isolated the vitamin in pure form, from rice polishings. Within a decade it was synthesized by Williams and Cline. Today it is not clear whether the neuritic symptoms are directly attributable to lesions of the nerves, or to functional interference due to the accumulation of metabolic products, particularly pyruvic acid. Wolbach states that on the whole, it seems best to regard the primary pathologic effects of "B_1" deficiency as not demonstrable at present — and to regard all the pathologic changes thus far recorded, including the myelin sheath lesions, as secondary effects. Notwithstanding the need for wholesome skepticism in the indiscriminate administration of "B_1", an impressive literature on its therapy is available. There are

several experiments which support the opinion that the diet of infants and children would be markedly improved by the use of thiamin. Warburg has demonstrated that riboflavin is the active group of an enzyme which appears to be present in varying amounts in practically all living cells and tissues. It appears that riboflavin is not synthesized by the animal cell; consequently, it must be supplied by the diet. It appears that nicotinic acid is but one of two or more substances essential for the prevention of pellagra. The animal body apparently cannot build this vitamin but must get it ready-made. Like thiamin and riboflavin, it is an indispensable agent in the enzyme system and is involved in certain biologic oxidations and reductions.

Wintrobe, Mitchell and Kolb[40] report that young pigs received an artificial diet presumably adequate in all respects. The quantity of yeast was gradually reduced in their diets and thiamin (B_1) and riboflavin were given in its place. Their rate of growth decreased, their general condition became impaired, and marked ataxia without motor weakness developed. Histologically the posterior columns of the spinal cord, dorsal root ganglion cells and the peripheral nerves showed severe degeneration.

Brandenburg[7] reports a case of severe bilateral tinnitus which followed extensive radiation therapy for carcinoma of the cervix uteri. The tinnitus was relieved by daily intravenous injection of "B_1" in doses of 10 to 15 mgs. for nine days. Brandenburg suggests that similar treatment may prove of value in neuropathies of the cranial nerves.

Veasey, Jr.[6] has presented a careful review of the literature on the vitamin B Complex. The historical data go back to the recognition by the Chinese of beriberi as a disease, in 2600 B.C. Cook, the explorer, attributed it to dietary faults; and a Japanese naval officer reduced the incidence of beriberi in 1872 by improving the diet. McCollum and Davis in 1914 found a water-soluble substance essential to growth and identical with Funks' vitamin. derived from rice polishings. In 1932, Cody described rhinological manifestations of "B" deficiency. These were frequent postnasal discharge, occasional sneezing, abnormal appearance of the mucosa over the middle turbinate, and a creamy white appearance of tips of turbinates. The laboratory procedures for detecting the need of

"B" therapy are not yet fool-proof. Harris considered that a 140 lb. man with 12 International Units of "B_1" per day in the urine, who failed to increase his urinary output with 500 International Units, was suffering from "B_1" deficiency. The daily requirement of "B_1" appears to be about 1 mg. However, since it has been repeatedly pointed out that our dietary is low in "B_1" — by Borsook and Sure and others — various points are to be considered. These are the refining of foods; the greater increase of cost in foods containing "B_1"; variation in individual requirements; and the inability to utilize or absorb the vitamin because of gastrointestinal conditions.

In a recent article, Cowgill[41] computes the relation of "B_1" to calories. According to his reckoning, the minimal adult requirement of 300-500 International Units (I.U.) daily, corresponds to about 10 I.U. per 100 calories daily. There is a higher demand in the case of pre-school children, namely 20 to 25 I.U. per 100 calories daily. Flour produced by modern milling processes contains much less "B_1" than that ground between stones a century ago. The present output has in it only about one-eleventh of what the flour provided by the old method. When one considers that one-quarter or more of today's caloric consumption is furnished by cereal foods, the tremendous decrease in "B_1" intake becomes serious indeed. Moreover white sugar, lamentably deficient in vitamin value, is consumed in increasingly larger amounts. Cowgill calls for the addition of "B_1" to our daily diet, in sufficient amounts to effect the restoration of "B_1" potency in wheat products to a level of 1000 to 1200 I.U. daily — far above the present level of 450 to 550 I.U.

Goodhart and Sinclair[42] present evidence to show that the amount of cocarboxylase in blood, determined by a clinical method, varies directly with the amount of total "B_1", determined by a biological method, and also with the degree of saturation of the tissues with the vitamin. It has been proved that "B_1" acts as a catalyst necessary for the breaking down of pyruvate, only after it has been converted into cocarboxylase. The authors have shown that definite deficiency of "B_1" is not uncommon among hospital patients in England. They also emphasize that vitamin deficiencies in man are almost always multiple and are therefore usually inadequately treated by administration of a single pure vitamin.

Platt and Lu[43] state that the pyruvate level in normal human blood is of the order of 0.5 mg. in 100 cc. of blood. When the level of blood pyruvate remains high, it is to be associated, in fulminating types of beriberi, with "B_1" deficiency.

Vorhaus[44] reports his results of a five year study of 520 cases of polyneuritis treated with thiamin chloride. Sixty-one per cent of these became symptom free, 36 per cent were partially improved and 3 per cent were unimproved. For 505 cases treated for nine weeks, following which the treatment was discontinued, recurrence of symptoms occurred in 62.5 per cent; 71 per cent of 111 cases under observation from one to two years after discontinuing thiamin showed recurrence. Readministration of thiamin was found to be highly effective in the treatment of recurrence of symptoms.

Wilder and Rutledge[29] note that the different components of the B Complex differ widely — chemically, physiologically and in their clinical behavior. In crystalline form we now have available "B_1", nicotinic acid and "B_6". Of these factors in the B Complex, thiamin and nicotinic acid have been found to be of great therapeutic importance in man; while riboflavin and "B_6" have not yet been definitely identified as of therapeutic importance. "B_1" — a daily intake of 1 to 2 mg. in food by adults apparently satisfies the requirement of man for this substance. It seems established that in 1840, the British and Americans consumed about three times the amount of "B_1" that is taken by the average American today. It seems probable that beriberi is really endemic in this country; and that, at least in mild form, the "B_1" deficiency includes an appreciable part of our whole population — due of course to our "refined" foods. States of riboflavin deficiency have not been reported in man; and over-doses apparently are not toxic.

The chemical nature of riboflavin attracted the attention of chemists as early as 1879 — (Booher[45]). No unusual significance was associated with this pigment by the early workers who apparently regard it only as one of the minor constituents of milk. Riboflavin has been isolated from a wide variety of animal and plant products, including egg white, milk, liver, kidney, urine, barley malt, dandelion blossoms, grasses, egg yolk and the retinas of fish eyes. It cannot be

stated definitely that the crystalline flavin obtained from each of these various sources is chemically identical with riboflavin, but such is the case at least for those to which adequate determinative tests have been applied. The riboflavin requirements are closely related to the body size, or more particularly to the mass of tissue — a further fact which may help to explain some of the divergence in vitamin values reported for riboflavin. Its rôle as a component of an oxidation enzyme, present presumably in all living cells, explains some of the observations which were so baffling only a few years ago. Riboflavin is concerned with the chemical reactions involved in cell respiration.

Hogan:[46] There seems to be no dispute — riboflavin has some function in the oxidization processes of the cell. The flavin content of organs cannot be much increased; even a tenfold increase in the amount of riboflavin consumed, increases very slightly the amount of it in the liver. On the other hand, the body guards its store of this substance and even in rats that die for lack of it, the amount in the kidney, liver and heart is still about one-third of the normal level. Excretion, in man: — If the consumption of riboflavin is greatly increased there is a corresponding increase in the amount eliminated. On a very low intake the excretion exceeds the intake. On a high intake the excretion relatively lags behind. It is estimated that a man should receive from 2 to 3 mgs. of riboflavin daily. It is also estimated that a cow may consume 50 mgs. of riboflavin in one day and secrete 10 liters of milk, containing 1 mg. per liter — thus giving a recovery of 20 per cent. Riboflavin deficiency has not yet been reported in man. Apparently, the presence of riboflavin in the retina is helpful when the illumination is not intense. The human eye has only 1/100 of the amount of riboflavin that is found in the eye of the codfish.

The dietary sources of riboflavin are presented by Sherman and Lanford.[47] Certain individuals, the poor in particular, do not consume enough vitamin A and riboflavin to insure the state of nutrition essential to the greatest physical stamina, efficiency and ability to resist infectious diseases. Riboflavin appears to be formed primarily in the green leaves of actively growing plants and to remain there in higher concentration than elsewhere in the plant. The concentration of riboflavin in the green leaves presents an interesting contrast

to the transfer of carotene (from which vitamin A is evolved) from leaf to root. In the carrot, the riboflavin remains in the leaves; the carotene goes from the leaves to the roots.

Oden, Oden and Sebrell[48] discuss riboflavin: In 1938, Sebrell and Butler reported the experimental production of lesions due to riboflavin deficiency, in the angles of the mouth, on the lips, and around the nose and eyes. The most characteristic changes were reddened, macerated lesions in each angle of the mouth, which progressed to transverse linear fissures. The lips had a reddened, denuded appearance, and there was a scaly, slightly greasy dermatitis around the nasolabial folds and in some cases around the eyes and ears. Three cases with lesions similar to those described above were found in a rural section of Georgia. These lesions receded under treatment with a daily dose of 5 mgs. of synthetic riboflavin. As the authors have seen many such cases in their practice, they consider that ariboflavinosis is, in all probability, a common dietary-deficiency disease in the southern United States.

Since 1933, Jolliffe, Fein and Rosenblum[49] have observed in fifteen patients the characteristic skin and mucous membrane lesions now believed to be a manifestation of riboflavin deficiency. Facial lesions consist of filiform excrescences, seborrheic in nature and apparently derived from the sebaceous glands, ranging in length up to 1 mm. Closely to sparsely scattered over the face, they resemble urea frost, but cannot be brushed off by the fingers. In addition there are fissures and maceration at the angles of the mouth and crust formation on the epithelium of the lips. Occasionally the vestibule of the nose is involved. These lesions respond to riboflavin (50 mgs. intramuscularly for 1 or 2 days with 10 mgs. by mouth daily) — but not to nicotinic acid.

In dogs with a "B_2" deficiency, Zimmerman[50] found marked demyelinization of peripheral nerves, and degeneration of axis cylinders. Many medullary sheaths and axis cylinders of the posterior columns were destroyed by gliosis. These changes were similar to those found in human pellagra.

Frostig and Spies[51] discuss "B_1" and nicotinic acid: Nutritional deficiencies widespread in a population may not only weaken the physical strength, but may also break down the morale. Subclinical beriberi or pellagra may be an important

factor in the fighting morale of any army, supporting Napoleon's contention that "an army marches on its stomach". Since nutritional deficiencies may be related to neurotic manifestations, examination for the nervous symptoms of such deficiencies should become a matter of routine psychiatric tests. Administration of large amounts of either thiamin or nicotinic acid, under controlled conditions, will aid in establishing the correctness of the diagnosis. Sixty patients with subclinical and mild pellagra and associated deficiencies were examined and special attention given to their subjective symptoms. The symptoms were found to be uniform, and they had no connection with the personality. These patients appear to have anxiety states with depressive features. The etiology of this syndrome was established by the administration, under controlled conditions, of large amounts of "B_1", nicotinic acid, or cocarboxylase. Despite the clear-cut manner in which these substances are specific, the usual case should have, in addition, a well-balanced diet. They found that riboflavin and "B_6" did not produce the same effect.

Aring, Evans and Spies[52] state that it is often difficult to make a diagnosis of "B_1" deficiency with any degree of assurance, but this may be remedied shortly by simple diagnostic laboratory methods. Treatment: (1) Fresh foods — potatoes, native vegetables, pork, liver, eggs, milk, fruits; beans and whole grain cereals, instead of decorticated cereals and dried or canned foods; (2) Dried yeast, wheat germ, liver, kidney and "B_1" crystals. The expense often interferes with their extensive use. The optimal dose in nicotinic acid therapy symptoms, at least 500 mgs. a day is given by mouth in ten equal doses. They have given as much as 2000 mgs. daily without untoward results. There may occur some flushing and feeling of warmth in the skin.

Spies, Bean and Vilter[53] investigated the properties of adenylic acid by administering it to normal persons and to persons with mixed deficiency diseases. Adenylic acid is a constituent of the pyridine dinucleotides, coenzymes I and II, and is widely distributed in nature. They found as follows: (1) Pellagrins in relapse are benefited by treatment with nicotinic acid and adenylic acid; (2) Six patients with malnutrition, who had intense burning of the oral mucous membranes, but no diagnostic evidence of pellagra, were relieved by adenylic acid alone; (3) However, since severe reactions

were produced by the intravenous injection of three preparations of adenylic acid, they do not recommend that this compound be administered to human beings. These studies indicate that some of the symptoms of mixed vitamin deficiency are relieved by adenylic acid. This compound, in some cases, may act in a manner similar to riboflavin in increasing the effectiveness of nicotinic acid in pellagrins in relapse. This finding gives further evidence not only of the multiple and mixed nature of deficiency diseases in human beings, but also suggests that they are the result of dysfunction of certain fundamentally related enzymes.

The outstanding development in nutrition during the past two years has been due to the discovery of the effect of nicotinic acid in pellagra, (Wilder and Rutledge[29]). The importance of this discovery is difficult to estimate, when one considers the number of pellagrins in this country and the rapidly curative effect of such an inexpensive substance as nicotinic acid. The experimental dose is 0.5 gm. in five 0.1 gm. doses daily.

Everyone knows that pellagra is present in the southern part of this country and is to be found particularly in poor people. Evans[54] considers that there are many cases which occur in other states and in other population groups. He presents a series of cases which were not typical pellagra, but he made the diagnosis because of the prompt response to nicotinic acid. Before the discovery of nicotinic acid therapy, he had noted many cases of glossitis and stomatitis which were not explainable on the basis of uremia, anemia or infection. He treated these with brewers' yeast and liver extract, but the results were slow and doubtful. Later when he gave nicotinic acid to cases of a similar type, the glossitis and stomatitis responded promptly. The buccal and oral membranes became normal in a day or two, thus clinching the diagnosis of pellagra. In some cases, although the physical symptoms of pellagra promptly responded to nicotinic acid, there was not a marked change in the mental condition; in other cases the mental disturbances promptly responded to nicotinic acid. Diarrhea in four cases, vaginitis in three, abdominal pain in four, fever in three, stomatitis and glossitis in thirteen and dermatitis in one — these all responded promptly to nicotinic acid. All these patients were adequately cared for financially, but they had inadequate diets. The

author believes that there are probably many cases of atypical and subclinical pellagra in Chicago; this disease was found in thirteen of 205 cases admitted to a private sanitarium.

Recent developments have indicated that nicotinic acid may prove to be a valuable agent in the treatment of pellagra. Sebrell[55] has observed improvement in mucous membrane lesions within twelve hours after administering nicotinic acid. Many consider, however, that nicotinic acid is not the sole deficiency in pellagra.

Emerson, Mohammad, Emerson and Evans[56] were successful in concentrating "B_6" from a wheat germ autolysate or cane molasses in neutral or acid solution. It was extracted with butyl alcohol as its picrate, and further concentrated; then the inert material was removed with acetone and ethyl alcohol. "B_6" was precipitated with phosphotungstic acid.

Spies, Bean and Ashe[57] reported on the favorable response of four pellagrins to a selected diet supplemented with thiamin, riboflavin, nicotinic acid, and a single 50 mgs. dose of "B_6". Without the latter, the patients failed to recover entirely.

Fouts, Helmer, Lepkovsky and Jukes[58] found that puppies show a normal rate of growth on purified casein diets, supplemented with concentrated "B_1", crystalline riboflavin, liver extract (containing the chick antidermatitis factor and nicotinic acid), and rice polish extract (containing the rat antidermatitis factor, vitamin B_6). Severe microcytic hypochromic anemia developed when "B_6" was the only missing component of the diet. The anemia was cured by the addition to the diet of this missing factor. Black tongue was produced in puppies whenever the liver extract (nicotinic acid and chick antidermatitis factor) was absent from the diet.

Since "B_6" is a constituent of liver and yeast, both of which relieve some of the symptoms of pellagra and pernicious anemia in relapse, Vilter, Schiro and Spies[59] decided to give large amounts of synthetic "B_6" to pellagrins with macrocytic anemia and to patients with classical pernicious anemia. Their findings indicate that "B_6", when administered in large amounts, has a definite effect upon the hematopoietic system of human beings who have the macrocytic anemia of pellagra

or pernicious anemia in relapse. In their opinion, this substance does not act specifically either as the true anti-pernicious factor or as the extrinsic factor of Castle.

Pantothenic acid was first shown to be an important vitamin in animal nutrition by Jukes, Woolley, Waisman and Elvehjem. Gyorgy, Poling and Subbarow[60] report the following: When a basal diet deficient in "B" and supplemented with "B_1" and riboflavin, is fed to rats, certain skin manifestations may persist or develop anew, after the specific acrodynia has been moderated or cured by treatment with pure "B_6". These lesions may be sores about the mouth, and scaly dermatitis in the axillae, groin and over the back between the scapulae. Alopecia follows and extends to the neck and over the back. Occasionally there is an exfoliative dermatitis. These skin manifestations are promptly cured by proper doses of liver, yeast, filtrates from wheat germ extracts, and rice polishings. The curative factor, therefore, must be part of the filtrate factor. A purified but still crude zinc salt of pantothenic acid proved effective in the cure of the lesions and in the promotion of growth.

The "anti-gray hair" component of the filtrate factor was found by Doctor Agnes Fay Morgan[61] and her associates in the Department of Home Economics of the University of California. When this factor is lacking in the diet of dark or black haired rats, patches of gray hair appear; and gradually the animals assume an appearance of senility. It is possible that this factor, contained in sugar cane molasses and other foods may be related to processes common to the ageing of man. In a later article, Morgan and Simms[62] give up-to-date information: Young black or hooded rats, fed on a diet adequate in all respects except for vitamins of the "B" group, received in addition thiamin chloride, riboflavin and a wheat germ preparation rich in "B_6". They grew fairly well and in 6 to 10 weeks developed gray fur. Filtrates from Fuller's earth-treated extracts of rice bran, yeast, liver, crude cane molasses and alfalfa improved their condition in every case, but restored normal growth in varying degrees. It appears that two filtrate factors are involved — the anti-gray hair factor and the rat growth factor. An histologic study of the adrenals, thyroids, skin and testes, showed serious damage in the gray rats. The results suggest a relation between

senescent changes, and one of the members of the "B_2" complex, upon which normal function of the cortical adrenal and other glands is dependent.

Ono[63] in 1928, described changes in the ears of experimental animals, with avitaminoses B and C. Particular attention was paid to the degenerative changes in the axis cylinders and myelin sheaths of the VIII Nerve, in both vestibular and cochlear branches, in vitamin B deficient animals. Irregular thickenings and minor changes were described for the axis cylinders, and moderate to extreme demyelinization. In "C" deficient guinea pigs, he noted the presence of hemorrhage in the middle ear, bony changes in the capsule, but, a normal appearance of the nerve.

Perla[64] notes that scattered evidence reported in the literature indicates increased frequency of spontaneous infection in animals and man, fed on diets deficient in vitamin B. This is dependent on alterations in cellular metabolism and also on atrophic changes secondary to the polyneuritis. "B" deficiency in dogs, pigeons and rats lowers their natural resistance to subsequently induced bacterial and nematode infection. There are many inconsistencies at present. "B" is essential in the process of oxidation in brain and nerve tissue; it plays a significant rôle in growth particularly in the young.

VITAMIN C.

Wilder and Rutledge[29] emphasize the importance of vitamin C, because of its clearly established rôle of maintaining the physical state of intercellular material. Because of this function, "C" is closely related to the metabolism of calcium and to the growth of bones, teeth and many tissues, such as cartilage and white fibrous tissue. The need of man for "C" can be stated more accurately than for any of the other vitamins. The principal methods by which the requirement is determined are the resistance or fragility of blood capillaries; the excretion of ascorbic acid in the urine; and the content of ascorbic acid in the blood. From 50 to 60 mgs. for adults may be considered to be the average necessary level of daily consumption. Treatment with "C" is generally simple. Foods rich in "C" form the basis for any therapeutic approach.

Curative doses of crystalline preparations vary from 30 to 1000 mgs. daily. Overdosage is not harmful.

Morch[27] states that hypovitaminosis C may be associated with hypovitaminosis A; and that the latter may mask the hypovitaminosis C.

Signs:

1. Gingivitis and hemorrhages.

2. Reddening of the mucous membrane of pharynx and larynx.

3. Eruption — papular, between fingers and also in other locations.

4. Considerable lassitude.

5. Dyspepsia.

Too intense a treatment with Vitamin C.

1. Obstruction of nasal fossae — sensation of pressure or pain at root of nose.

2. Lassitude and nervousness.

3. Increased intestinal motility.

4. Occasionally a peculiar type of skin eruption.

Case: Man aged 36 yrs., agriculturist, with more or less typical Ménière's symptoms, and evidence of hypovitaminoses A and C. Treatment. For four months he received injection of 40,000 units of vitamin A and 4 cc. of Ascortrine. The latter contained to each 2 cc., 10 mgs. citrine (Ido) and 100 mgs. ascorbic acid. The ascorbic acid value in the serum (Lind and Lieck) at the beginning of the treatment was 25 mgs.%; and 3 mos. later was in the neighborhood of 85 mgs.%. At that time most of his symptoms had disappeared. Six months later he was symptomless.

Case: 42 yr. old farmer; had spells of vertigo for two months previously, but no vomiting or nausea. Following the last spell, he had tinnitus in the left ear. There were no subjective or objective symptoms of "A" deficiency. For a long time he had had gingival hemorrhages and other signs of "C" deficiency. This man received 2 cc. of Ascortrine which was

repeated 4 times, at ten day intervals. After the fourth and last injection, the patient's symptoms entirely disappeared; but he had a slight headache which lasted for some time. He then received as a maintenance dose Ido (vitamin C) — 5 grs. daily. This contained 2.5 mgs. ascorbic acid to 1 grain of Ido. He has had no further complaints.

Case: 26 yr. old agriculturist, unmarried. He had been in the hospital off and on for ten years for "Ménière treatments" by the method of Mygind. After each series of treatments, the symptoms would disappear for about 1 month. This patient had vertigo, some deafness, nausea and vomiting and some tinnitus. There was evidence of both "A" and "C" deficiency. He received 1 cc. of Avital and 4 cc. of Ascortrine. After the last injection he had no complaints.

Case: 44 yr. old butcher. This patient had arterial hypertension, chronic rhinopharyngitis, laryngitis, tracheitis, deafness and vertigo. He received 1 cc. of Avital, and 2 cc. Ascortrine at weekly intervals for 3 weeks. All symptoms practically disappeared and his blood pressure dropped from 220/110 to 145/85. After the treatments he was to continue with 2 tablets of Avital and 5 gr. of Ido C per day.

Glasunow[65] states that the osteoporosis of scurvy is the result of fibrous atrophy of bone. Scurvy is a disease of the entire mesenchyme, characterized by a loss of the property of differentiation on the part of the newly formed mesenchyme.

By inviting Harris[66] to contribute something "suggestive and provocative" to a volume of essays presented to Sir Frederick Gowland Hopkins, the editors prepared the ground for a stimulating article. In controlled examinations of the excretion of "C" in urine, he observed that patients suffering from such diseases as (1) acute rheumatism, (2) surgical tuberculosis, (3) pulmonary tuberculosis, (4) osteomyelitis, and (5) rheumatoid arthritis, excrete notably less than the control subjects; the former are in a state of much lower "saturation" than the latter, and little of the large test doses of "C" overflows into the urine. He regards the urine test as possibly having some diagnostic and prophylactic value in the presence of an infective process. In isolated coastal communities in Scandinavia, respiratory infections are common in the spring and the winter seasons, in which no fruit or

vegetables are available; but their incidence drops off after a cargo of fruit and other fresh foods has been landed. A low intake of "C" can diminish the resistance to infection; however, it is not yet clear that, once an infection has started, massive doses of "C" can act against the infection. To "C" may be ascribed a special function in stimulating the growth of formative cells in general.

VITAMIN D.

Friedmann[67] remarks that those who consider biochemistry as applied chemistry, can justify this view by pointing to the brilliant results in the fields of hormones and of vitamins. Isolation of adrenalin, thyroxin, sex hormones, and of vitamins A, B_1, B_2, C and D is a successful accomplishment equal to anything done in other fields of biochemistry. The method followed in these researches was the same in all but one case. The hormones and the vitamins were isolated very often as a result of large-scale work possible only through the help of broadminded and far-seeing industrialists. For vitamin D, another road was traveled. In 1906, Hopkins suggested that rickets was due to some deficiency of nutrition. Some years later, Funk and Macallum induced a ricket-like condition in chicks by administering an incomplete diet. The disease could be cured with cod-liver oil. They assumed that a vitamin present in cod-liver oil was responsible. Following this, Mellanby, McCollum, Sherman and Pappenheimer proved that rickets is a deficiency disease. In 1919, Huldschinsky discovered that sunlight, and especially ultra-violet ray, had curative properties in human rickets. In 1924, Hess and Steenbock found that a great number of foodstuffs, having no antirachitic properties, became antirachitic after irradiation with sunlight or ultra-violet ray. The substance so activated by sunlight was called "provitamin D".

In their recent book — "Vitamin D" — Reed, Struck and Steck[68] cover the literature as well as present the results of their own work. First, in speaking of the general subject of vitamins, they mention how broad is the field of interest for those concerned with medicine and allied branches, chemists, nutritional experts, veterinarians, workers in animal husbandry and agricultural specialties, game and fish experts — constituting a field whose scope is rarely equalled by that of

any group of substances related to life-processes. It is recognized that there are several substances which may be classed as "vitamins D" — because of their antirachitic properties. While chemically related, they have slightly different physiologic properties. The authors mention 12 members of the "D" group and state that still other forms may exist. Rickets is still a common disease. Moore and his collaborators examined over 900 children in two American cities and found that over 90 per cent showed evidence of present or past rickets; even the children living in San Diego, a city with abundant sunshine all the year, showed as much rickets as those living in Portland, Oregon, a city subject to many prolonged cloudy spells. The disease is widespread among city children, particularly those from the lower-income group. The mild cases are relatively unimportant; and yet, if unchecked, may well become serious in later years. Far more important is the effect of a deficiency of "D" on growth. The optimal dose for good growth is definitely above the minimal protective dose for rickets. Therefore, a mild degree of rickets with no clinical signs except X-ray, is not to be dismissed lightly as harmless, since it must surely have a distressing effect upon growth. It appears that the parathyroids are not primarily concerned in rickets. From the evidence now available it appears that "D" directly influences the absorption of calcium and indirectly, the absorption of phosphorus. Severe and even fatal intoxication may be produced by excessive amounts of "D". There is a tendency to deposition of calcium and, to a less extent, of phosphorus in soft tissues. This process is reversible to a considerable extent and apparently leaves no chronic injury. The threshold of intoxication for human subjects and dogs appears to be 20,000 units per kilogram of body weight per day. Of all tissues studied, the kidney appears to be the most vulnerable, and the aorta next. Nevertheless, hypertension has never been encountered in human subjects. There is some evidence in favor of beneficial influence of "D" in combating infections, but proof that this is anything more than an effect on general nutritive conditions is not conclusive. A group of 45 cases of atrophic arthritis, 7 of hypertrophic arthritis and 3 mixed cases were treated with 150,000–200,000 units of "D" daily; there was definite measurable improvement in 74.5 per cent of these cases, as manifested by reduced swelling and

pain, increased mobility, improved muscular tonus and gain in weight.

Wilder and Rutledge[29] report that apparently the main action of "D" is to increase the absorption of calcium and phosphorus or to diminish their intestinal excretion. Naturally a proper intake of "D" is of greatest importance for infants and children. For adolescents it seems that a need for "D" does exist. For adults the optimal amount, if indeed a need exists, remains to be determined. During pregnancy and lactation, however, a dosage of 800 units or more is suggested.

Snyder and Squires[69] had observed 23 cases of severe chronic arthritis — over a two year period, during which no improvement resulted from various forms of therapy. They then tried "D" therapy in high dosage — a relatively high percentage of the patients showed marked and sustained clinical improvement — although the laboratory tests and X-ray findings revealed no clear correlation to explain the subjective and objective improvement.

In three patients, Albright and Sulkowitch[70] studied the actions of "A. T. 10" and "D" on the calcium and phosphorus metabolism. In one patient, the action of parathyroid hormone was studied. It was found that both the "A. T. 10" and "D" had the same fundamental actions — to increase calcium absorption from the gut and to increase phosphate excretion in the urine. "A. T. 10" resembled parathyroid hormone in that it caused a markedly increased urinary excretion of phosphates; the hormone, however, differed in that it appeared to have no primary action on calcium absorption by the gut.

VITAMIN E.

The chemical substance termed vitamin E, first discovered by Herbert M. Evans, is now purified as alpha-tocopherol. Shimotori, Emerson and Evans[71] found that alpha-tocopherol acts effectively in preventing muscular dystrophy, in experimental animals.

Telford, Emerson and Evans[72] reported on the histologic changes in the skeletal musculature of the young of rats paralyzed by a diet low in "E". They found a progressive degeneration of the muscle, which was correlated with the severity

of the paralysis. Various claims have been made as to the influence of "E" upon the thyroid and pituitary glands. These findings have not been generally confirmed. "E" has been used with considerable success in cases of habitual abortion, in the human; pregnancies have frequently followed the administration of "E".

Bicknell[73] shows two processes to be concerned in the muscular dystrophy of "E" deficiency. One involves the nervous and the other the muscular system. There is degeneration of the posterior columns and anterior horn cells, accompanying the muscular degeneration. The latter can be shown to regress with "E" therapy.

Wechsler[74] states that the treatment of two cases of amyotrophic lateral sclerosis responded to 3 mg. doses of "E" three times daily.

VITAMIN K.

Wilder and Rutledge[29] state there has been much recent interest in a possible relation between a deficiency of vitamin K and the hemorrhagic tendency in jaundice. It seems that "K" may be of importance in maintaining a normal concentration of prothrombin; and that it has to do with the fabrication, storage or activation of prothrombin which occurs in the liver. Apparently when administered to jaundiced patients, "K" must be given, plus bile or bile salts. Emulsions of this vitamin have been used intramuscularly with the return to normal of the clotting power of the blood — (Dam and Glavind[75]).

In 1935, Quick, Stanley-Brown and Bancroft[76] found a deficiency of prothrombin in patients with jaundice. The next year Schonheyder[77] examined the blood of chicks, deficient in "K" and found that the prolonged clotting time of the blood was due to a diminution in thrombin. In this way, it was found that "K" is effective in the treatment of the hemorrhagic diathesis which is noted in obstructive jaundice.

Doisy, Binkley, Thayer and McKee,[78] in their review of studies on vitamin K, state that sources of it are widely distributed in green leaves and vegetables. Certain foods such as rice bran and fish meal, stored under moist conditions, develop "K"; hence a large number of bacteria synthesize

a substance having "K" activity. "K" deficiency was discovered to have a prolonged clotting time of the blood in deficient chicks. This was due to diminution in thrombin. Many reports have dealt with the effects of "K" in obstructive jaundice, in which absorption from the intestine is impaired because of a lack of bile. Also many studies have been carried out in the treatment of spontaneous and traumatic hemorrhage of the newborn. The prothrombin level of the blood of babies is subnormal in amount. Although recent, the results of clinical application of this vitamin are already encouraging.

VITAMINS IN GENERAL.

Gildea[79] discusses the recognition of early symptoms of deficiencies. Lack of vitamins disturbs the whole function of the body. The earliest symptom may be only a loss of appetite or lack of energy. Then one or more of the following systems will break down: *1.* Skin may show slight atrophy, scaling and pigmentation and if not treated, may progress to ulceration. *2.* Nervous system. The symptoms begin as paresthesias and pain and are followed by weakness and paralysis. Mental disturbances are not uncommon. *3.* Alimentary tract. Anorexia and stomatitis are the first symptoms; these may be followed by: Atrophy of the tongue, achlorhydria, and diarrhea. Ulceration of the intestine may develop in severe cases. *4.* Hematopoietic system may be the one first affected. Macrocytic or microcytic or hypochromic anemia may develop, depending on the kind of deficiency and on the patient. *5.* Cardiovascular. Irregularities or rapid pulse rates constitute early signs of vagus nerve involvement. *6.* Disturbed carbohydrate metabolism may produce ketosis and phenyl pyruvic acid in the urine. This latter early sign is now thought to be the fundamental clue to the action of "B_1". The present conception is that "B_1" is necessary in the metabolism of carbohydrates. It apparently serves as a co-enzyme in the disposal of pyruvic acid and indirectly of lactic acid.

Cowgill[80] notes that in order to limit our variables properly, and to work as far as possible with a diet lacking only the factor of interest, it is pertinent to ask what factors are needed for satisfactory nutrition. At least 32 known material factors are required. These are: ten essential amino acids;

essential fatty acids; twelve inorganic or mineral nutrients; and at least eight vitamin factors, *viz:* A, B_1, B_2, nicotinic acid, C, D, E, B_6 and vitamin K. Certain other factors such as vitamin B_4, the filtrate factor and factor W must also receive consideration.

In addition to the specific individual substances just mentioned, the student of nutrition must take account of the energy factor, the calories needed for vital activity, and the number of calories actually consumed by the selected mixture of protein, carbohydrate and fat. Furthermore, if the alimentary tract is to exhibit a normal motility, some consideration must be given the factor of indigestible residue or "bulkage".

In most studies of vitamin deficiencies the experimental animals exhibit some degree of anorexia. If, as has been pointed out, over 32 different substances are needed for satisfactory nutrition, and the animal fails to eat the desired amount of the experimental ration, it is quite possible that in addition to the vitamin deficiency of interest, there will occur some degree of lack of one or more other factors. For this reason it is important to institute what has been called the inanition control. This control animal is fed the same diet but only in amounts determined by the voluntary food intake of the experimental animals the day before. The control animal, however, receives the vitamin which is withheld from the experimental. Failure to recognize the importance of this control makes the results of many studies questionable.

* * *

Having presented the opinions and findings of a few of the many who are doing research work on the vitamins, we are fortunate in receiving from Dwight Wilbur[81, 82, 83] his attempt to make a clinical summary of the entire matter. He emphasizes that information on this subject is being added so rapidly that it is impossible for any one individual to keep in touch with the progress that is now being made in the scientific study of the vitamins. The charts which he has prepared give us a summary in graphic form. Reviewing these again and again, helps to fasten in one's mind the distinctions between the various vitamins. The following will

give his general comments, his summary and his graphic charts:

We now know that disease may be due to a deficiency of vitamins; this concept has received widespread proof and is universally accepted. Our clinical interest now lies in determining the presence of a deficiency. There is one fact peculiar to such disease — if only we can learn how to detect the beginnings of a deficiency, such disease can be entirely prevented; and, except in a few extreme instances, it can be completely cured. In order to have a clearer understanding of deficiency diseases and of the difficulties in recognizing them, the following table is of value:

TABLE 1.—THE CHARACTER OF VITAMIN-DEFICIENCY STATES.

Degree of Deficiency	Clinical Signs	Essential Changes	Incidence	Diagnosis
Marked	Classical Deficiency Disease	Extensive Pathologic	Rare	Clinical findings
Moderate	Variable	Pathologic and Physiologic	Occasional	Clinical findings Laboratory tests
Mild	Absent? Preclinical?	Physiologic	Common	Laboratory tests

Those with a marked deficiency present a classical disease, such as xerophthalmia, beriberi or pellagra. Such conditions are due to definite pathologic changes in the tissues; they can be recognized by clinical means without recourse to special tests, but they are rarely seen in this country.

Those with a moderate degree of deficiency, may exhibit such conditions as the multiple neuritis of chronic alcoholism, night blindness, certain types of macrocytic anemia and glossitis. In such cases the diagnosis depends upon clinical findings, in some instances supplemented by laboratory tests. It would seem probable that a vitamin deficiency is present in an appreciable number of our patients.

Those with a mild deficiency may give no clinical signs nor show any pathologic changes. The diagnosis rests largely on the laboratory tests, such as biophotometric determination of dark adaptation of the eyes, in "A" deficiency; and the chemical measurement of the saturation of tissues with "C." Unfortunately, we do not yet have many laboratory tests to

help in the diagnosis of these mild deficiencies. Even now, however, a therapeutic test may be of value as a diagnostic procedure; some of the vitamins are available in crystalline form and a specific response, after using such a pure form of vitamin may be considered significant in establishing the diagnosis.

DEFICIENCY IN "A". The most readily noted clinical symptoms have to do with changes in the eyes — such as night blindness or inability to see clearly in dusky light, and of irritation or lesions of the conjunctivae. In its most exaggerated form, xerophthalmia (which is rarely observed in this country), there may be dryness of the conjunctival tissues, conjunctivitis, softening of the cornea, infection of the eyeball, and blindness.

The principal interest is in the detection of states of moderate or of mild deficiencies, in which the clinical diagnosis is not easy. If the clinical history suggests an "A" deficiency, the patient should be tested: (1) For the sensitivity to light; (2) Scrapings can be made from the conjunctival, nasal or vaginal mucous membranes — making smears and examining them for keratinized epithelial cells; (3) Administration of "A" for the therapeutic test.

A deficiency of "A" may be prevented by eating adequate amounts of butter, cream, eggs, cod-liver oil, carrots and spinach. Fish-liver oils, particularly rich in "A", are those of the halibut, cod, burbot, and tuna. Daily optimal requirement is not known, but it is probably between 6,000 to 10,000 units. Treatment of "A" deficiency: (1) Diet containing many foods rich in "A"; (2) Supplements of "A" in cod-liver or halibut-liver oil — 10,000 to 25,000 units daily; (3) In rare instances by intramuscular injection of cod-liver oil or other substances rich in "A".

DEFICIENCY IN "B_1". Thiamin, a catylist, essential for the oxidation of carbohydrates. When it is not present in adequate amounts in man, there occur peripheral neuritis, circulatory failure and beriberi. While symptoms of a deficiency of "B_1" may be sudden in onset, they are generally insidious; the earliest manifestations usually are heaviness in the legs and tenderness of the calf muscles.

TABLE 2.—THIAMIN DEFICIENCY (VITAMIN B_1).

Degree of Deficiency	Clinical Signs	Incidence	Tests
Marked	Beriberi	Rare	
Moderate	Peripheral neuritis Cardiovascular disturbances Edema Gastrointestinal dysfunction?* Anemia?*	Infrequent	1. Calculations Cowgill's Formula 2. Therapeutic 3. Amounts of Thiamin in blood and urine
Mild (Preclinical?)	Uncertain mild degree of above	Unknown	

*Changes in these organs are very frequently associated with thiamin deficiency, but are probably due to deficiency of components of the vitamin B complex other than thiamin.

The diagnosis is simple if the patient exhibits the characteristic symptoms of beriberi, namely, peripheral neuritis, edema and cardiac failure. The diagnosis of a moderate deficiency is not so difficult as it was a few years ago; for example, we know that peripheral neuritis is usually due to "B_1" deficiency. A lack of "B_1" is usually present in chronic alcoholics, among patients who have been on a limited diet as a result of poverty, faddism, ignorance or in an attempt to reduce weight, and during pregnancy and lactation. Treatment: An adequate diet rich in "B_1", preparations of brewers' yeast or wheat germ, and crystalline thiamin itself. Crystalline thiamin should not be used exclusively — because most patients have a deficiency of other components of the B Complex; and because thiamin is still quite expensive. Dosage: For those with a moderate deficiency and without evidence of impairment of gastrointestinal function — 30 gms. of powdered brewers' yeast, or 6 gms. of autolyzed yeast, three times a day. Along with this should be a high caloric, high vitamin diet; and from 10 to 40 mg. of thiamin daily — given orally or intramuscularly.

DEFICIENCY IN "B" (other than thiamin). The B complex consists of a variety of factors other than thiamin: riboflavin; the Pellagra-Preventive — or P.P. factor (which is now usually considered to be nicotinic acid); a filtrate factor; "B_6" and others. However, up to this time only two members of the B complex, thiamin and the P-P factor, have been linked unquestionably with deficiency disease in man.

TABLE 3. — VITAMIN B DEFICIENCY (Other than in Thiamin).

Clinical Changes	Deficiency of	Tests
Pellagra	Nicotinic acid Thiamin Other factors?	Therapeutic only
Macrocytic anemia	Uncertain	Therapeutic only
Gastro-intestinal: glossitis, anorexia, achlorhydria, hypotonicity, hypomotility	Uncertain	Therapeutic only

Deficiency of the P-P factor (nicotinic acid?) produces pellagra — the characteristic symptoms of which are the three D's — diarrhea, dementia and dermatitis. These three occur simultaneously in severe cases only. The most characteristic feature is the dermatitis without which the diagnosis is questionable.

TABLE 4. — NICOTINIC ACID DEFICIENCY.

Degree of Deficiency	Clinical Signs	Incidence	Tests
Marked	Pellagra	Rare in North Common in South of the United States.	1. Therapeutic
Moderate	Mild pellagra 1. Nervous or mental symptoms 2. Gastrointestinal symptoms 3. Cutaneous lesions	Unknown	2. Abnormal pigments in urine?
Mild	Pre-clinical or above in indefinite and vague forms	Unknown	

While diagnostic and laboratory tests are not yet developed, the therapeutic test with nicotinic acid is proving of considerable diagnostic value.

Mild degrees of deficiency are not clear-cut and little is known about them. Treatment. Daily requirement is unknown; nevertheless the treatment of pellagra has been very effective. A diet high in calories, proteins and the vitamins, supplemented by nicotinic acid in doses of 500 to 1000 mgs., thiamin chloride in doses of 20 to 50 mgs., powdered brewers' yeast in doses of 75 to 150 gms. or the dilute

liver extract. The requirements of certain vitamins are given in the following chart:

TABLE 5. — THE REQUIREMENTS OF THE VITAMINS.

Vitamin	Units	Child	Adult	Pregnancy and Lactation	Optimal	Therapeutic
B_1 Thiamin	IU*	300-450	300-600	750-900	600	3000-30,000
	mg.	1.0-1.5	1.0-2.0	2.5-3.0	2.0	10.0-100.0
Nicotinic acid	mg.	?	25x	?	?	200-500
B_2(G) Riboflavin	mg.	?	2-3x	?	?	2-10x
B_6	mg.	?	?	?	?	?

*International Units. (x) Suggested amounts.

DEFICIENCY IN "C". The fundamental pathologic change is in the intercellular substance, particularly of the blood vessels — with consequent hemorrhage into the subcutaneous, subperiosteal, gingival and other tissues. The clinical diagnosis of "scurvy" is relatively simple in a well developed case; but is not so easy in cases of latent or preclinical scurvy. The diagnosis may be suspected in patients who have unexplained hemorrhages of any type or in any situation, who have long-continued infections, or who have considerable dental caries. Such conditions do not establish the diagnosis of "C" deficiency, but suggest the possibility of it. Fortunately, we possess better methods of determining the presence or absence of a partial deficiency of "C" than of any other vitamin. These methods include the capillary resistance test; X-ray of bones; the intradermal test; studies of the levels of "C" in plasma and of the excretion of "C" in the urine; and the "C" tolerance tests.

Treatment. Deficiency in "C" may be avoided by intake of a diet adequate in fresh fruits, particularly of the citrus variety, and vegetables; the minimal intake is not certain, but probably approximates 20 to 40 mgs. daily. In the treatment of a deficiency, the diet should be high in its content of the above mentioned foods, supplemented by "C" in synthetic crystalline form by mouth or intravenously, in doses of from 50 to 200 mgs. In case of hemorrhage in which rapid action is desired, larger doses, such as 1000 mgs. may be given daily for two or three days and then reduced to levels of from 100 to 300 mgs. daily until the condition is cured.

DEFICIENCY IN "D". "D" is the "antirachitic" vitamin and plays an essential rôle in metabolism of calcium and phosphorus; it has to do in particular with the retention of calcium and phosphorus in the body, in the deposit of these substances in bones and, perhaps, in the concentration of these elements in the blood.

TABLE 6. — VITAMIN D DEFICIENCY.

Degree of Deficiency	Clinical Signs	Incidence	Tests
Marked	Rickets Osteomalacia	Common Rare	1. X-ray of bones
Moderate	Rickets Dental caries Inadequate mineralization of bone Tetany	Common (50-90 per cent of infants)	2. Blood phosphatase 3. Therapeutic
Mild (Preclinical?)	Uncertain (Above in milder forms?)	Unknown	

Rickets is such a widespread condition in infancy (50 to 90 per cent of infants are stated to have it) that it may be classified as probably the most common deficiency disease. "D" deficiency in adults may lead to osteomalacia, but this is very rare in the United States. It is probable that certain forms of osteoporosis, of tetany, and possibly of dental caries, are the result of "D" deficiency, either because of an inadequate diet or because of interference with absorption of "D" or of calcium from the intestine.

The diagnosis of rickets is usually simple. In cases where the symptoms are less clear-cut, the diagnosis may be suspected clinically and confirmed by X-rays of the bones. Further confirmatory evidence may be obtained by the determination of the blood phosphatase, which is usually increased in rickets. The therapeutic test in the administration of "D" may be helpful in establishing the diagnosis.

Treatment. There are two sterols known to be of prime importance — activated ergosterol or calciferol, and 7-dehydrocholesterol, which is the chief sterol of animal fats. In the treatment of rickets, a dose of twenty drops of viosterol (4500 units) or a similar number of units of "D" in another form, is effective. "D" may also be supplied by fish-liver oils; irradiated yeast; milk and cereals; milk to which a con-

centrate of Vitamin D has been added; or by irradiation of the skin.

DEFICIENCY IN "E". At least three substances possess the effect of "E". It has not yet been clearly demonstrated that any of them is required by man for normal health or in reproduction. Of principal clinical interest is the possible rôle of deficiency in "E", in threatened and spontaneous abortion, and of an excess of "E" found in malignant disease.

DEFICIENCY IN "K". Known as the antihemorrhagic factor, "K" may play a rôle in the production of prothrombin. In certain animals, a "K" deficiency leads to a decrease in the prothrombin content of the blood. "K" is not available on the market, but substances rich in it are green vegetables, pig-liver fat, hemp seed, and alfalfa.

Wilbur makes a final comment: Too much stress cannot be placed on the importance of an adequate diet in the prevention and treatment of deficiency disease.

TABLE 7. — PROTECTIVE FOODS WHICH SERVE AS A FOUNDATION FOR A NORMAL DIET
(Daily Quantities).

Milk	1 pint
Egg	1
Vegetables	3 large servings, besides potatoes (one a green leafy vegetable)
Fruit	2 servings (one raw)
Meat, fish or fowl	1 serving (about 2 ounces)
Butter	1 tablespoonful

In the treatment of some deficiency states, crystals and concentrates of some of the vitamins are available; but, while these products are extremely useful, they should always be supplemented by vitamins in the natural state — in foods, yeast, cod-liver oil; not only because this is the way in which vitamins ordinarily are obtained by normal persons, but especially because there are present in foods certain essential substances which have not only not been synthesized or concentrated, but of which at present we are only vaguely aware.

* * *

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BIBLIOGRAPHY.

1. STRAUSS, MAURICE B.: The Therapeutic Use of Vitamin B_1 in Polyneuritis and Cardiovascular Conditions, The Vitamins, A. M. A., pp. 193-202, 1939.

2. SHURLY, B. R.: Deficiency Diet in Relation to the Skeleton, Especially in Connection with the Bone Affections of the Head, *Annals of Oto. Rhino. and Laryn.*, 38, 612-621, 1929.

3. SHURLY, BURT R. and TURNER, R. G.: Infection of Accessory Sinuses and Upper Respiratory Tract in Vitamin A Deficiency, *Jour. A. M. A.*, 94: 539-543, 1930.

4. LEWIS, E. R.: Biochemistry and Clinical Backgrounds, *Trans. of the American Laryn. Rhino. and Otolog. Soc., Inc.*, pp. 458-464, 1939.

5. MOOSE, RAY M.: Revelations of Detailed Diet Histories Obtained in the Practice of Ophthalmology and Otolaryngology, *Archives of Otolaryngology*, 21: 64-70, 1935.

6. VEASEY, CLARENCE A. JR.: Nature of Vitamin B and Its Components, *Archives of Otolaryngology*, 31: 74-93, 1940.

7. BRANDENBURG, K. C.: Relief of Neuritis of VIII Cranial Nerve with Vitamin B_1, *Archives of Otolaryngology*, 31: 189-191, 1940.

8. SELFRIDGE, GRANT: Chronic Progressive Deafness from a Nutritional Standpoint: a Preliminary Report, *Annals of Otol., Rhino. and Laryn.*, 46: 875-894, 1937.

9. SELFRIDGE, GRANT: Eighth Nerve High Tone Deafness from a Nutritional Standpoint, *Annals of Oto., Rhino. and Laryn.*, 46: 93-118, 1937.

10. SELFRIDGE, GRANT: Nicotinic Acid and the Eighth Nerve. A Preliminary Report, *Annals of Oto., Rhino. and Laryng.*, 48: 39-53, 1939.

11. SELFRIDGE, GRANT: Eighth Nerve High Tone Deafness from a Nutritional Standpoint (a further contribution), *Annals of Oto., Rhino. and Laryn.*, 48: 608-631, 1939.

12. SELFRIDGE, GRANT: The Present Status of Vitamins in Relation to VIII Nerve and Conduction Deafness. An unpublished report, 1940.

13. COVELL, W. P., and NOBLE, L.: The Significance of Myelin Sheath Degeneration for the Cochlear Nerve, *Annals of Oto., Rhino. and Laryn.*, 46: 895-911, 1937.

14. COVELL, W. P.: Histopathologic Changes in the Peripheral Auditory Mechanism for Experimental Vitamin Deficiencies. Read before the Research Study Club of Los Angeles, Los Angeles, California.

15. LOCH, W. E.: Veränderungen der Labyrinthkapsel bei Tierexperimentellen Avitaminosen (A, C, D, E). *Monatsschr. f. Ohren. u. Laryngo-Rhinol.*, 8: 542-561, 1939.

16. GUGGENHEIM, LOUIS: "Otosclerosis," Louis Guggenheim, 1935.

17. GUGGENHEIM, LOUIS: The Diagnosis and Treatment of Otosclerosis, *American Journ. of Surgery*, Oct., 1938.

18. GUGGENHEIM, LOUIS: Lectures before the Mid-Winter Course of the Research Study Club, Los Angeles, 1939-40.

19. MCLESTER, JAMES S.: Foreword in book entitled Vitamin B_1, by Williams and Spies, The Macmillan Co., N. Y., 1938.

20. FISHBEIN, MORRIS: Introduction in the book, The Vitamins, A.M.A., pp. 1-13, 1939.

21. BESSEY, OTTO A. and WOLBACH, S. B.: Vitamin A — Physiology and Pathology, The Vitamins, A.M.A., pp. 27-54, 1939.

22. CLAUSEN, S. W.: The Pharmacology and Therapeutics of Vitamin A, The Vitamins, A.M.A., pp. 55-86, 1939.

23. MUNSELL, HAZEL E.: Vitamin A — Methods of Assay and Sources in Food, The Vitamins, A.M.A., pp. 87-109, 1939.

24. BOOHER, LELA E.: Vitamin A Intake Requirements and Practical Recommendations for Vitamin A, The Vitamins, A.M.A., pp. 111-125, 1939.

25. MELLANBY, EDWARD: Xerophthalmia, Trigeminal Degeneration and Vitamin A Deficiency, *J. Path. and Bact.*, 38: 391, 1934.

26. ZIMMERMAN, H. M., COWGILL, G. R. and FOX, J. C.: Neurologic Manifestations in Vitamin G (B_2) Deficiency, *Arch. Neurol. and Psychiat.*, 37: 286-306, 1937.

27. MORCH, P.: Traitement de la maladie de Ménière et d'autres affections s'accompagmant de bourdonnements otogenes et de vertiges par les vitamines, *Acta Otolaryngol.*, 28: 629-637, 1939.

28. WOLBACH, S. B. and BESSEY, O. A.: Relative Overgrowth of the Central Nervous System in Vitamin A Deficiency in Young Rats, *Science*, 91: 599-600, 1940.

29. WILDER, RUSSELL M. and RUTLEDGE, DAVID I: Diseases of Metabolism, reprint from *Archives of Internal Medicine*, 63: 356-427, 1939.

30. MELLANBY, EDWARD: The Experimental Production of Deafness in Young Animals by Diet, *J. Physiol.*, 94: 380-398, 1938.

31. NELSON, E. M.: The Components of the Vitamin B Complex, The Vitamins, A.M.A., p. 127, 1939.

32. WILLIAMS, ROBERT R.: The Chemistry of Thiamin (Vitamin B_1), The Vitamins, A.M.A., p. 141, 1939.

33. COWGILL, GEORGE R.: The Physiology of Vitamin B_1, The Vitamins, A.M.A., p. 159, 1939.

34. WRIGHT, MARGARET D. and BAKER, AUDREY Z.: Vitamin B_1 Excretion on a Varied Intake, *Journ. of Hygiene*, 39: 638-642, 1939.

35. VEDDER, E. B.: The Pathology of Beriberi, The Vitamins, A.M.A., p. 179, 1939.

36. MUNSELL, HAZEL E.: Vitamin B_1, Methods of Assay and Food Sources, The Vitamins, A.M.A., pp. 203-227, 1939.

37. WILLIAMS, R. R. and SPIES, T. D.: Vitamin B_1 and Its Use in Medicine, a book published by the Macmillan Co., N. Y., 1938.

38. ZIMMERMAN, H. M. and BURACH, E.: Vitamin B_1 Deficiency, *Arch. Path.*, 13: 207, 1932.

39. BECKER, J. ERNESTINE: Recent Vitamin Research, II. Vitamins C, B Complex and the Less Well Known Vitamin Factors, *Journ. Am. Dietetic Assn.*, 16: 16-33, 1940.

40. WINTROBE, M. M., MITCHELL, D. M. and KOLB, L. C.: Neuron Degeneration in Vitamin Deficiency, *Journ. Exp. Med.*, 68: 207, 1938.

41. COWGILL, GEORGE R.: The Need for the Addition of Vitamin B_1 to Staple American Foods, *Journ. A.M.A.*, 1939.

42. GOODHART, R. and SINCLAIR, H. M.: Deficiency of Vitamin B_1 in Man, as Determined by the Blood Cocarboxylase, *Journ. of Biolog. Chemistry*, 132: 11-21, 1940.

43. PLATT, B. S. and LU, G. D.: Studies on the Metabolism of Pyruvic Acid in Normal and Vitamin B_1 Deficient States. The Accumulation of Pyruvic Acid and Other Carbonyl Compounds in Beriberi and the Effect of Vitamin B_1, *The Biochemical Journal*, Vol. XXXIII, pp. 1525-1537, 1939.

44. VORHAUS, MARTIN G.: Evaluation of Vitamin B_1 (Thiamin Chloride) in the Treatment of Polyneuritis, *The Am. Journ. of the Med. Sciences*, 198: 837-844, 1939.

45. BOOHER, LELA E.: Chemical Aspects of Riboflavin, The Vitamins, A.M.A., pp. 249-270, 1939.

46: HOGAN, A. G.: Riboflavin: Physiology and Pathology, The Vitamins, A.M.A., pp. 271-288, 1939.

47. SHERMAN, HENRY C. and LANFORD, CAROLINE SHERMAN: Riboflavin: Dietary Sources and Requirements, The Vitamins, A.M.A., pp. 289-295, 1939.

48. ODEN, J. W., ODEN, L. H. JR. and SEBRELL, W. H.: Report of Three Cases of Ariboflavinosis, *Public Health Rep.* 54, 790-792, 1939.

49. JOLLIFFE, N., FEIN, H. D. and ROSENBLUM, L. A.: Riboflavin Deficiency in Man, *New Eng. J. Med.*, 221, pp. 921-926, 1939.

50. ZIMMERMAN, H. M.: Lesions of the Nervous System in Vitamin Deficiency, *J. Exp. Med.*, 57: 215-228, 1933.

51. FROSTIG, J. P. and SPIES, T. D.: The Initial Nervous Syndrome of Pellagra and Associated Deficiency Diseases, *Am. Journ. Med. Sciences*, 199: 268-274, 1940.

52. ARING, CHARLES D., EVANS, JOSEPH P. and SPIES, TOM D.: Some Clinical Neurologic Aspects of Vitamin B Deficiencies, *Journ. of A.M.A.*, 113: 2105-2110, 1939.

53. SPIES, T., BEAN, W. B. and VILTER, R. W.: Adenylic Acid in Human Nutrition, *Annals of Int. Med.*, 13: 1616-1618, 1940.

54. EVANS, VERNON L.: Subclinical Pellagra in the Chicago Area; Its Incidence Among Cases Admitted to a Private Sanitarium, *Ill. Med. Journ.*, 76: 458, 1939.

55. SEBRELL, W. H.: Vitamins in Relation to the Prevention and Treatment of Pellagra, The Vitamins, A.M.A., pp. 297-321, 1939.

56. EMERSON, G. A., MOHAMMAD, A., EMERSON, O. H. and EVANS, H. M.: Steps in the Concentration of Vitamin B_c, *J. Biol. Chem.*, 124: 377-383, 1938.

57. SPIES, T. D., BEAN, W. B. and ASHE, W. F.: A Note on the Use of Vitamin B_c in Human Nutrition, *J. Am. Med. Assn.*, 112, p. 2414, 1939.

58. FOUTS, P. J., HELMER, O. M., LEPKOVSKY, S. and JUKES, T. H.: Production of Microcytic Hypochromic Anemia in Puppies on Synthetic Diet Deficient in Rat Antidermatitis Factor (vitamin B_c), *J. Nutrition*, 16: 197-207, 1938.

59. VILTER, R. W., SCHIRO, H. S. and SPIES, T. D.: Effect of Synthetic Vitamin B_c on the Haemopoietic System of Human Beings, *Nature*, 145: 388, 1940.

60. Gyorg, P., Poling, C. E. and Subbarow, Y.: Experiments on the Antidermatitis Component of the Filtrate Factor in Rats, *Proc. Soc. Exper. Biol. and Med.*, 42: 738-740, 1939.

61. Morgan, Agnes Fay, Cook, Bessie B. and Davison, Helen G.: Vitamin B_2 Deficiencies as Affected by Dietary Carbohydrate, *J. of Nutrition*, 15: 27-43, 1938.

62. Morgan, A. F. and Simms, H. D.: Graying of Fur and Other Distu-bances in Several Species Due to a Vitamin Deficiency, *J. Nutrition*, 19: 233-250, 1940.

63. Ono, T.: Experimentelle Histo-pathologische Studien des Gehörorgans bei der B und C Avitaminose, 1. Mitteilung, *Trans. Jap. Path. Soc.*, 18: 172-175, 1928.

64. Perla, B.: Role of Vitamin B in Resistance, *Arch. Path.*, 25: 540-568 and 694-729, 1938.

65. Glasunow, M.: Experimental Scurvy of the Guinea Pig, *Virch. Arch. f. Path. Anat.*, 299: 120, 1937.

66. Harris, Leslie J.: Vitamin C and Infection, Perspectives in Biochemistry, Cambridge University Press, pp. 329-336, 1938.

67. Friedmann, Ernst: Vitamin D, Perspectives in Biochemistry, Cambridge University Press, p. 244, 1938.

68. Reed, C. I., Struck, H. C. and Steck, I. E.: Vitamin D, a book published by the University of Chicago Press, 1939.

69. Snyder, R. G. and Squires, W. H.: A Preliminary Report on Activated Ergosterol, *N. Y. State Med. Journ.*, pp. 708-719, 1940.

70. Albright, F. and Sulkowitch, H. W.: The Effect of Vitamin D on Calcium and Phosphorus Metabolism, Studies on Four Patients, *J. Clin. Investig.*, 17: 305-315, 1938.

71. Shimotori, N., Emerson, G. A. and Evans, H. M.: Role of Vitamin E in the Prevention of Muscular Dystrophy in Guinea Pigs Reared on Synthetic Rations, *Science*, 90: 89, 1939.

72. Telford, I. R., Emerson, G. A. and Evans, H. M.: Reduced Muscle Creatine in Paralyzed Young E-low Rats, *Proc. Soc. Exper. Biol. and Med.*, 41:315-318, 1939.

73. Bicknell, F.: Vitamin E in the Treatment of Muscular Dystrophies and Nervous Diseases, *Lancet*, 1: 10, 1940.

74. Wechsler, I. S.: Recovery in Amyotrophic Lateral Sclerosis Treated with Tocopherols (Vitamin E): Preliminary Report, *J. Amer. Med. Assn.*, 114: 948, 1940.

75. Dam, H. and Glavind, J.: Clotting Power of Human and Mammalian Blood in Relation to Vitamin K, *Acta med. Scandinav.*, 96: 108-128, 1938.

76. Quick, Armand J., Stanley-Brown, Margaret and Bancroft, Frederic W.: A Study of the Coagulation Defect in Hemophilia and Jaundice, *Am. Jour. Med. Science*, 190: 501-511, 1935.

77. Schonheyder, Fritz: The Quantitative Determination of Vitamin K, *Biochem. Journ.*, 30: 890-896, 1936.

78. Doisy, E. A., Binkley, S. B., Thayer, S. A. and McKee, R. W.: Vitamin K, *Science*, 91: 2351, pp. 58-62, 1940.

79. GILDEA, E. F.: Vitamin Deficiencies with Special Reference to Those Involving the Nervous System, *The Connecticut State Medical Journal*, 4: 83-87, 1940.

80. COWGILL, G. R.: Vitamin Deficiencies and the Nervous System. A Consideration of the Contributions of Animal Experimentation, *The Yale Journ. Biol. and Med.*, 12, 205-212, 1940.

81. WILBUR, DWIGHT, L.: Diseases of Metabolism and Nutrition, reprint from *Archives of Int. Med.*, 63: 356-427, 1939.

82. WILBUR, DWIGHT L.: Vitamin-Deficiency States: Their Recognition and Treatment, *Calif. and Western Med.*, 50:184-187, 1939.

83. WILBUR, DWIGHT L.: Vitamin Deficiency States: Their Recognition and Treatment, *Calif. and Western Med.*, 50: 270-274, 1939.

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SIXTH ANNUAL MEETING, MISSISSIPPI VALLEY MEDICAL SOCIETY, ROCK ISLAND, ILL., SEPT. 25-27.

The Sixth Annual Meeting of the Mississippi Valley Medical Society will be held at the Hotel Fort Armstrong, Rock Island, Ill., Sept. 25-26-27. The program will be given by 32 clinician-teachers who will give over 60 lectures, demonstrations, round table discussions, etc. A special feature of the program this year will be 41 short instructional courses. Sept. 25, an all-Chicago program will be conducted by 10 well known clinician-teachers. Sept. 26, the annual banquet will be held. Sept. 27, short instructional courses will be given by faculty members from the University of Iowa. For further information, write the Secretary, Dr. Harold Swanberg, W. C. U. building, Quincy, Ill.

PATHOLOGIC CHANGES IN THE PERIPHERAL AUDITORY MECHANISM DUE TO AVITAMINOSES (A, B COMPLEX, C, D AND E).*†

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Although much remains to be accomplished before we have a definite knowledge of disorders of the ear, nose and throat due to vitamin deficiencies, nevertheless certain information is being accumulated. Unfortunately, with the exception of diseases such as beriberi, pellagra, scurvy and rickets, a clear-cut picture of a particular vitamin-lack does not exist for the human. Our greatest need is to come to recognize physical signs which accompany mild or moderate grades of a dietary deficiency. This is not an easy task — since it is highly probable that the diet of an individual shown to be deficient in one factor may also be lacking in other related vitamins. For example, to prescribe vitamin B_1 for nerve deafness without first ascertaining the possible relationship of the hearing impairment to a dietary deficiency, will lead only to discouraging results.

In previous articles (Covell[1, 2]), experimental deficiencies in several vitamins were shown to produce degeneration of the cochlear nerve. Since that time the studies have been further extended, as additional material has become available. The present report deals with the histopathologic changes in the peripheral auditory mechanism for avitaminoses A, B_1, B_2, B_6, filtrate factor (anti-gray hair factor and chick antidermatitis factor), C, D and E. The study cannot be considered complete in all details. Some of the experiments were conducted with relatively few animals. A longer interval on the deficient diets and the production of a truly chronic deficiency might reveal additional pathologic changes. However, for each avitaminosis, the results reported for all the series point towards specific changes in the ear. Of

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course, they are to be regarded as related only to the particular animals concerned in the experiments. It is hoped that further advancements in the rapidly changing field of vitamins may finally explain their influence upon metabolism, growth and normal functions of the human body. Of interest in this connection are the recent studies of Wolbach and Bessey[3] which demonstrate that in vitamin A deficient animals, bone growth lags behind that of the nervous system; hence unequal growth of the two systems results in distortion of nerve roots and herniations in the central nervous system. Little is known of the influence of vitamins on periods of prenatal development; and it is possible that many characteristics now considered of an hereditary nature may actually be dietary in origin. It may well be that certain types of congenital deafness will finally be explained on a nutritional basis.

MATERIAL AND METHODS.

Brief detail of the experimental procedure for each group of animals is given in the accompanying Table I. Most of the experiments were conducted in the laboratories of the Institute of Experimental Biology, University of California. The deficient and control animals were made available through the courtesy of Doctor Herbert Evans. The experimental chick material was obtained from Doctor T. H. Jukes, Division of Poultry Husbandry, University of California at Davis. The controls received the same diet as the deficient animals, with the exception that the missing factor was added to their diets. For several of the deficiencies, the animals were first allowed to show the characteristic manifestations following which they were fed the lacking vitamin for a period of several weeks. In this way the effects of repair of the previous damage could be estimated. Guinea pigs were used for vitamin C studies. Rats deprived of one of eight of the vitamins in their diets number 83 in all. There were 22 control rats which were usually litter mates of the vitamin deficient animals.

Both temporal bones of all animals and chicks were prepared for study according to the method outlined in a previous article (Covell[1]).

TABLE I.

A SUMMARY OF THE HISTOPATHOLOGICAL FINDINGS IN EXPERIMENTAL ANIMALS ON VARIOUS VITAMIN DEFICIENT DIETS.*

Experiment		Pathologic Changes	Comments	
Deficiency	No. of Animals	Middle Ear	Inner Ear	
Vitamin A	12 rats, 52 days on diet lacking in vitamin A. 4 rats received missing factor in diet.	Epithelial metaplasia of lining with keratinization and secondary infection. Penetration of exudate into tensor tympani muscle. Thickening of the periosteal layer of bone.	Degeneration of external sulcus cells, cells of stria vascularis (mitochondria **not** altered), scattered spiral ganglion cells. Slight to moderate demyelinization of distal part of nerve particularly in basal whoris. Exostoses in internal auditory canal (3 specimens).	The alterations in the ear accompanying vitamin A deficiency confirm the findings reported by Mellanby. It is doubtful that all nerve and spiral ganglion cell changes are the result of pressure by an exostosis in the internal auditory canal.
Vitamin C	4 guinea pigs, 26 days on a vitamin C deficient diet. 2 guinea pigs received vitamin C in diet.	Middle ear cavity filled with serosanguineous fluid. Hemorrhage into submucosa with proliferation of fibroblasts. Some sloughing of epithelium. Tendency for replacement of cellular marrow by fibrous type.	Swelling and degeneration of all cells in organ of Corti, external sulcus and some of stria vascularis. Accumulation of fluid between spiral ligament and bony wall. Demyelinization of nerve distally is slight. Endolymphatic duct widely patent.	Further experiments are in progress to determine the effects of a more prolonged and chronic vitamin C deficiency upon the ear.
Vitamin D	25 rats, 18-23 days on a vitamin D deficient diet. Followed by 8 days of treatment with tuna fish oil. Varying degrees of healing.	Otitis media (9 ears) with congestion in vicinity of eustachian tube (14 ears). Joints of ossicular chain unchanged. Osteoid about small vessels in bone of ossicles and otic capsule.	Animals killed with chloroform hence alterations in organ of Corti varied. Demyelinization of distal part of nerve slight to moderate.	The relatively high incidence of middle ear infections, the formation of osteoid in the periosteal and enchondral layers of the capsule and the degenerative changes in the cochlear nerve are results of this deficiency.
Vitamin E	3 rats, third generation on a vitamin E-low diet. 2 rats of same age which received vitamin E.	Low grade inflammatory reaction in submucosa with some sloughing of mucosa. Hemorrhage under submucosa. Small irregularities in form of new bone (periosteal). Degeneration of fibers in both intrinsic muscles.	Hemorrhage into scala tympani (1 ear), about nerve in modiolus and subdurally for all specimens. Small exostosis in modiolus (1 ear). 10% formalin fixation without perfusion, not suitable for study of changes in membranous cochlea.	Hemorrhage, middle ear inflammation, formation of small irregularities in the periosteal layer and degeneration of the fibers of the intrinsic muscles of the middle ear are the outstanding changes to be found in this material.

TABLE I (Continued).

A SUMMARY OF THE HISTOPATHOLOGICAL FINDINGS IN EXPERIMENTAL ANIMALS ON VARIOUS VITAMIN DEFICIENT DIETS.*

Experiment		Pathologic Changes	Comments	
Deficiency	No. of Animals	Middle Ear	Inner Ear	
Vitamin B_1	5 rats, 36 days on a diet lacking in vitamin B_1. 3 rats received thiamin chloride in diet.	4 ears revealed an otitis media while 3 showed an inflammatory reaction in vicinity of eustachian tube orifice. Degeneration of muscle fibers of tensor tympani with penetration of exudate into muscle.	External and internal hair cells were without alterations. Spiral ganglion cells were shrunken and deeply stained. Moderate to slight demyelinization in cochlear nerve always more in basal region.	The relatively high incidence of middle ear infection, alterations in the ganglion cells and myelin sheath are significant for this deficiency. Probably a more prolonged deficiency would yield changes of a drastic nature.
Vitamin B_1	5 rats, 14 days on a diet lacking in vitamin B_1. Followed by administration of thiamin chloride (5 micrograms) three times weekly for 82 days.	No changes in the lining of the middle ear cavity. Fibrous and fatty tissue replace many muscle fibers of the tensor tympani muscle.	No alterations of significant nature apparent in membranous cochlea. Demyelinization extremely slight or negligible.	The results for this group are in contrast to those of the above. Since these animals were deficient in vitamin B_1 for 14 days only, it is doubtful that changes of a serious nature were present in the cochlea.
Vitamin B_2	4 rats, 56 days on a diet deficient in flavin only. 6 rats received same diet except flavin added.	Moderate inflammatory reaction in lining of middle ear cavity, epithelium usually intact except for 2 ears with otitis media.	Hemorrhage into scala tympani for all specimens. Scattered external hair cells are degenerated. Stria vascularis cells swollen and vacuolated (2 ears). Spiral ganglion cells stain deeply and outlines shrunken. Moderate amount demyelinization of distal part of nerve.	Alterations for this group resemble those for avitaminosis B_1 but are more drastic in nature. The experiment was over a longer period of time than for the vitamin B_1 studies.
Vitamin B_2	5 rats, 69 days on a diet containing thiamin chloride and extract of rice bran (three times weekly). This diet was low in flavin.	7 ears revealed an otitis media, all showed congestion about middle ear orifice of eustachian tube. Exudate in middle ear penetrated between muscle bundles of stapedius and tensor tympani muscles.	Hemorrhage about nerve in modiolus in all specimens, none into scala tympani. External hair cells intact. Occasional spiral ganglion cell degenerated. Slight myelin sheath alterations.	Since this diet was low in flavin the findings were considerably less than for the above group. This diet may have also been lacking in other factors of the vitamin B_2 complex.
Vitamin B_2	4 rats, 28 days on diet containing no flavin, followed by 40 micrograms of flavin daily for 56 days.	Mild inflammatory reaction in submucosa (2 ears).	Very slight alterations in the myelin sheath of the nerve. No changes in the external hair cells. Spiral ganglion cells normal in appearance throughout.	The few changes described for this group probably represent incomplete healing after the missing factor was supplied in the diet for 56 days.

TABLE I (Continued).

A SUMMARY OF THE HISTOPATHOLOGICAL FINDINGS IN EXPERIMENTAL ANIMALS ON VARIOUS VITAMIN DEFICIENT DIETS.*

Experiment		Pathologic Changes		Comments
Deficiency	No. of Animals	Middle Ear	Inner Ear	
Vitamin B_6	6 rats, 28 days on diet deficient in vitamin B_6. 3 rats received same diet except missing factor added.	Otitis media (4 ears), labyrinthitis (2 ears).	External hair cells without significant changes. Cells of Deiter and external sulcus cells are swollen and vacuolated. Small groups of spiral ganglion cells are found to be altered. Myelin sheath degeneration is severe distally and moderate to slight proximally.	A lack of this vitamin caused the most drastic changes in the myelin sheath of any avitaminosis. The relatively high incidence of middle ear infection is also of importance.
Vitamin B_6	4 rats, 24 days on diet deficient in vitamin B_6. Followed by supplying missing factor in diet for 21 days.	Healing stages in otitis media (3 ears).	Slight degree of demyelinization present in distal portion of nerve. Probable loss of a few spiral ganglion cells. Otherwise no significant alterations.	This series of animals revealed practically no alterations after vitamin B_6 had been administered for 21 days. It is believed that the myelin sheath changes for these animals have been repaired.
Filtrate factor (antigray hair)	7 rats, 56 days deficient in filtrate factor. 4 rats received same diet except missing factor supplied.	Otitis media (3 ears). Old healed labyrinthitis (1 ear).	No alterations in external hair cells, swelling and vacuolization of external sulcus cells. Spiral ganglion cells shrunken and stain deeply. Moderate to slight demyelinization changes.	The lack of the "anti-gray hair" factor results in changes similar to those of avitaminosis B_6. They are less marked and particularly so since this experiment was of 56 days duration or twice as long as the vitamin B_6 deficiency.
Filtrate factor (antigray hair)	3 rats, 28 days on diet deficient in filtrate factor. Missing factor then supplied for 28 days.	No alterations of a significant nature.	Slight amount of demyelinization present in distal portions of nerve.	The alterations described for the above group seem to have been controlled by the administration of the missing factor for 28 days. It is doubtful that alterations of a marked degree were produced in the ear after 28 days on the deficient diet.

*The findings described under each group are for the vitamin deficient animals and were not in evidence for any of the controls which received the missing factor in their diet.

FINDINGS.

Rather than present the findings separately for each deficiency, the histopathologic changes of the various studies will be described under the headings of middle ear, membranous cochlea and cochlear nerve — thus making clear a comparison of the effects of the avitaminoses.

THE EXTERNAL EAR.

While attention has not been directed to the changes within the external ear and canal, only gross manifestations of the deficiencies are available for reporting. It seems worthy of mention that a deficiency in vitamin B_6 — the so-called "anti-dermatitis or anti-acrodynia factor" for the rat — causes a dermatitis of the external ear. In these animals it is not uncommon to find the greater part of the concha involved — or even lacking. Other deficiencies, with the exception of vitamin B_2 which may cause ulcerations, do not appear to attack the external ear. The chick "antidermatitis" factor results in lesions about the beak, while riboflavin deficiency produces "notched beak".

THE MIDDLE EAR.

The incidence of middle ear infection in the different groups on deficient diets, was considerably higher than in the controls. The reaction on the part of the mucosa and submucosa of the middle ear cavity was not of a typical or specific nature for most of the avitaminoses. In vitamin B_6 deficiency half of the ears revealed otitis media or labyrinthitis. The administration of the particular missing factor appeared to reduce the incidence of infection for avitaminoses B_1, B_2, B_6 and the filtrate factors. In the third generations of the vitamin E-low rats, the submucosa contained numerous inflammatory cells; and for one animal a typical otitis media was present. Changes of a more specific nature occurred in the lining of the middle ear cavity for animals deficient in vitamins A and C. Accompanying avitaminosis A, there was keratinization and metaplasia of the epithelium. Secondary to these changes, infection occurred. In vitamin C deficient guinea pigs, there was hemorrhage into the submucosa with fibroblastic proliferation and sloughing of the

epithelium. Figure 1 illustrates the appearance of the mucosa for avitaminosis C.

The muscles of the middle ear revealed varying degrees of alterations and degenerative changes in the fibers. Figure 2 shows the fibrous and fatty tissue replacement of the muscle bundles in the tensor tympani of a vitamin E deficient rat. More extensive degenerative changes were found in this muscle than in the stapedius muscle. Alterations of this type were consistently present in the vitamin E deficient animals.

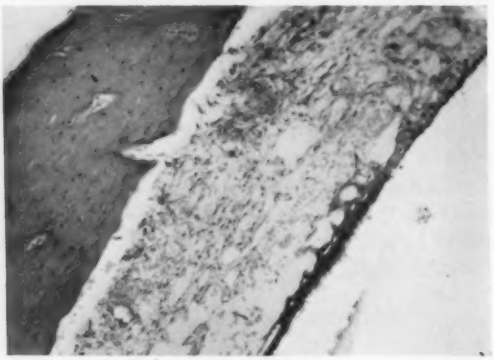

FIGURE 1.

Lining of middle ear cavity of a guinea pig deprived of vitamin C for a period of 26 days. There is hemorrhage into the submucosa, proliferation of fibroblasts and sloughing of the epithelial cells. Regaud fixation, hematoxylin and eosin. X120.

These may be related to the dystrophic changes found elsewhere in the muscles of these animals. Quite frequently the exudate of a middle ear infection penetrates and destroys some of the muscle bundles, so that the final picture is similar to the changes encountered for avitaminosis E. This may explain the occurrence of degenerated fibers, particularly for the tensor tympani, to be seen in some sections of human temporal bones.

The ossicular chain in vitamin A and E deficiencies revealed a thicker periosteal layer. For "E" deficiency this was evidenced by small irregularities on the surface of each ossicle. In vitamin A deficiency, it consisted of an actual increase in thickness of the periosteal bone covering the ossi-

cles. The bony substance of the ossicles contained unripe bone, in avitaminosis D animals. Osteoid was also present in the periosteal and enchondral layers of the otic capsule. There was a tendency for fibrous tissue replacement of any cellular marrow occurring in the ossicles, in vitamin C deficient animals. The ossicular joints were not altered by a lack of any vitamins in the diet. It may become possible to demonstrate changes in these chronically deficient animals, such as Rinehart[4] has found for avitaminosis C in other joints of the guinea pig. It is also of interest to point out

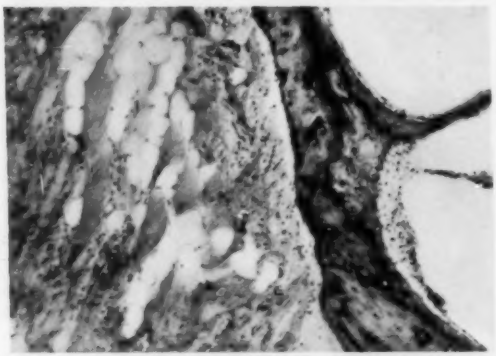

FIGURE 2.

Section through the tensor tympani muscle of a rat on a vitamin E-low diet. There is fibrous and fatty tissue replacement of the muscle bundles. Changes of a similar nature were found in other deficiencies subsequent to the presence of an inflammatory exudate in the middle ear which penetrated into the muscle. Formalin fixation, hematoxylin and eosin. X120.

that the stapediovestibular joint is unchanged with avitaminoses. Although alterations in the periosteal layer may extend up to the immediate vicinity of the joint, it has never been found to be involved.

MEMBRANOUS COCHLEA.

Degenerative changes in the membranous cochlea were not of an extreme type for any of the avitaminoses studied. Except in the occasional specimens (particularly of the vitamin B_6 group, which revealed a labyrinthitis), the organ of Corti, stria vascularis and external sulcus cells appeared to be intact. Significant alterations of a mild or moderate

degree were to be found in these various specialized cells of the cochlear duct. From the functional standpoint, the changes might well be considered as causing impairment of hearing — since they were not in evidence in control animals.

The organ of Corti revealed slight to moderate degenerative changes of its external hair cells for "B_2" deficiency. The internal hair cells did not show similar changes. In these flavin deficient animals, hemorrhage into the scala tympani

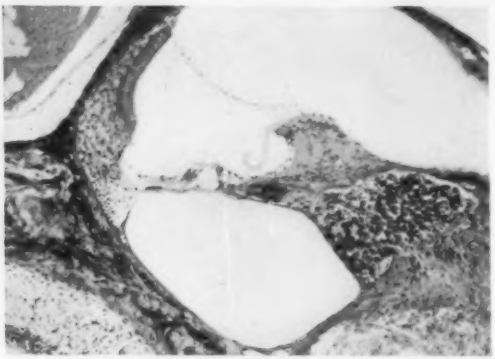

FIGURE 3.

Section through the lower turn of the cochlea of a vitamin B_1 deficient rat. This animal was maintained on a thiamin chloride free diet for 36 days. There is swelling of the external sulcus cells, the organ of Corti is intact and the spiral ganglion cells are slightly shrunken with an affinity for eosin stain. Regaud fixation, hematoxylin and eosin. X120.

for the lower turns of the cochlea was not an uncommon finding. It is possible that its presence within the vicinity of the hair cells had some untoward effect upon their appearance. The lower turns of the cochlea revealed more of these altered sensory cells; and their distribution was somewhat scattered. Figure 4 serves to illustrate this. In vitamin C deficient animals, the cells comprising the organ of Corti were swollen and stained evenly with eosin. Varying degrees of degeneration for the cells of Deiter, Claudius and Hensen were found in animals whose diets lacked the filtrate factor, vitamin B_6 and "A". The external sulcus cells showed mild to moderate changes for all deficiencies except in the deficiency for "C" which showed severe changes. The organ of Corti of a "C" deficient guinea pig is illustrated in Figure 5.

In vitamin A deficient animals, the stria vascularis was swollen and the cells exhibited degenerative changes. Although the cells were severely affected, nevertheless the mitochondria remained normal in shape and in staining reaction. Less obvious alterations were found in vitamin C deficient animals. Only an occasional cell showed changes similar to those encountered in an "A" deficiency. In "C" deficient guinea pigs, the spiral ligament was frequently found to be partially separated from the inner bony wall of

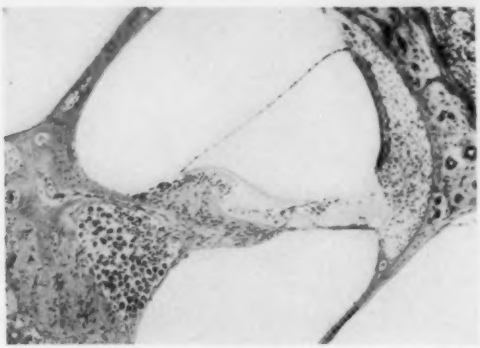

FIGURE 4.

Section through the lower turn of the cochlea of a vitamin B_2 deficient rat. This animal received a diet adequate in all respects except flavin of which it was deprived for 56 days. There is considerable swelling of all cells of the organ of Corti and external sulcus cells. The external hair cells show moderate degenerative changes. The alterations in the spiral ganglion cells are marked and some appear to be lacking in the lower turns of this cochlea. There was slight hemorrhage into the scala tympani for all flavin deficient animals which is not in evidence in this particular section. Regaud fixation, hematoxylin and eosin. X120.

the cochlea; Reissner's membrane was often ruptured; and the endolymphatic duct was widely patent. Such findings are usually to be attributed to poor fixation or postmortem autolysis; but since the control animals did not reveal them it seems certain that vitamin C deficiency results in changes of this nature.

SPIRAL GANGLIA.

The cells of the spiral ganglia are particularly subject to autolytic changes. While they serve as invaluable guides in studying the damage of any particular agent, caution must

be exercised in interpreting their appearance. They were found to be mildly influenced in most of the dietary studies. Changes were more in evidence for "B_2" deficient animals (Fig. 4), less for "B_1" (Fig. 3) and the filtrate factor, and considerably less for "A" and "B_6" (Fig. 6) deficiencies. Small groups of cells appeared to have undergone moderate changes in the latter animals. The appearance of the spiral ganglion cells was considerably improved for those animals

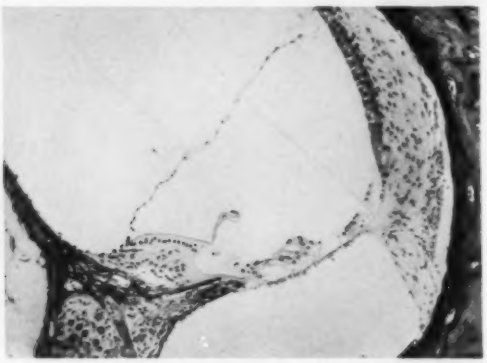

FIGURE 5.

Section through the second turn of the cochlea of a vitamin C deficient guinea pig. This animal was deprived of vitamin C for 26 days. Swelling and degeneration in all cells of the organ of Corti and external sulcus. Certain cells of the stria vascularis are vacuolated. Reissner's membrane is not intact. Spiral ligament is partially detached from the bony wall. These changes were definitely in contrast to the controls which received adequate amounts of vitamin C in their diets. Modified Marchi method counterstained with cresyl violet. X120.

which received the missing factors, after having rendered them deficient in vitamins B_1, B_2, B_6 and filtrate factor. Although a comparative count of the number of cells was not made, it is possible that an increased length of time on some of the deficient diets might cause the disappearance of large numbers of cells.

THE COCHLEAR NERVE.

It was previously shown (Covell[1]) that the extreme peripheral part of the nerve — or the dendritic fibers distal to the spiral ganglion cells — were more prone to changes in the myelin sheath than the proximal or axonic portion. It was

further observed that demyelinization of the cochlear nerve was considerably greater than that of other cranial nerves and even the vestibular portion of the VIII Nerve. These observations on the effects of quinine, sodium salicylate, a staphylococcus toxin and various vitamins on the myelin sheath of the cochlear nerve are of interest in view of this more comprehensive study of the vitamins. These changes will be summarized since the accompanying Table I gives the data for each group of deficient animals.

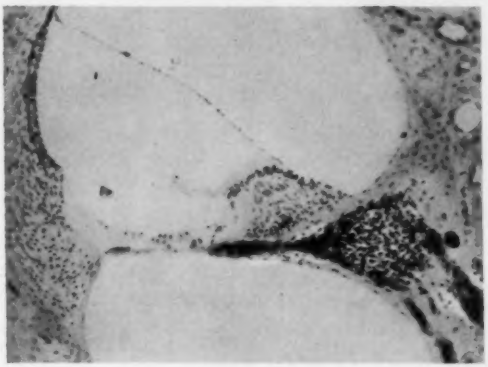

FIGURE 6.

Section through the second turn of the cochlea of a rat deprived of vitamin B_6 in its diet for a period of 28 days. The intense black staining in the osseous lamina is due to the reaction of the osmic acid on the degenerated myelin sheath of the dendritic part of the cochlear nerve. Modified Marchi method counterstained with cresyl violet. X120.

Demyelinization of the distal portion of the cochlear nerve was in evidence for all deficiencies. It was greatest for animals on a diet lacking in one of the vitamin B group factors. In order of their relative importance in producing these changes in the myelin sheath, avitaminosis B_6 (Fig. 6) revealed drastic alterations; less noticeable alterations were found for avitaminoses B_1 and B_2. The filtrate factor (anti-gray hair component) when not included in the diet of the rats, resulted in only slight demyelinization. Avitaminoses A and D showed a similar slight demyelinization. The least amount of change was found in vitamin C deficiency. No results are available as yet for vitamin E-low animals, nicotinic acid or vitamin K deficiencies.

A group of 9 chicks deficient in the antidermatitis portion of the filtrate factor were studied after employing technical methods similar to those used for rats. When compared to a group of 6 normal chicks, similarly treated, those on a deficient diet were found to have slight to moderate demyelinization of the lagenar branch of the nerve, while the vestibular portion showed relatively few alterations.

Two chicks maintained on a diet low in riboflavin for 3 months finally received the missing factor in their diets for a period of 3 weeks. All obvious signs of the deficiency had disappeared except a "peculiar jerking movement of the head and neck". In spite of their having received a full supply of riboflavin in their subsequent diets, the lagenar and vestibular branches were drastically altered in these birds.

A group of vitamin B_6 chicks included 4 deficient birds and 2 controls. The "B_6" deficiency was of comparatively short duration lasting only 20 days. Demyelinization changes were very slight. These experiments on chicks illustrate several important features regarding the type of conclusions to be drawn from experiments of short duration, or acute deficiencies, as compared to chronic and more prolonged deficiencies. Evidence obtained from the latter type of experiments is probably of greater importance for comparison with human cases of dietary deficiencies.

DISCUSSION.

These findings are presented, not with the end in view of immediate clinical application, but rather to emphasize the need for clinical studies of the ear, nose and throat. An excellent method of approach in clinical practice is outlined in the twelve points of I. H. Jones.[5] Selfridge[6] has made an attempt to discover the relation between vitamins and improvement in hearing. His results are encouraging. On the whole, the great field of dietary diseases of the nose and throat remain uninvestigated up to the present time. This is perhaps a more promising field for study than the problem of deafness. For example, changes in the mucous membrane of the nose due to vitamin A deficiency must offer less resistance to invasion by bacteria; and surely the pathway of infection for certain neurotrophic viruses is rendered more susceptible.

These studies confirm, in general, the findings of Mellanby,[7] Ono,[8] Loch[9] and others on the effects of various avitaminoses on the peripheral auditory mechanism. Emphasis has been laid upon the deficiencies included under the vitamin B group. Many of these have a common source in nature, such as the wheat germ. Our dietary is low in the latter because of the extent to which our cereals and flours are refined. It is in fact probable that the average human being is low in B vitamins. Since these vitamins have been shown to be essential for the maintenance of the functions of the central and peripheral nervous systems, certain cases of nerve deafness may well be due to their lack. As a rule, it will more probably meet the need to prescribe concentrates of the whole vitamin B group rather than a single factor.

The animal experiments include all the deficiences known for the different factors in the B_2 complex, with the exception of nicotinic acid. The latter deficiency is only successfully produced in dogs and such material was not available for study.

Attempts have not yet been made to study the auditory pathways in the central nervous system either for the effects of drugs, toxins, chemicals, or dietary deficiencies. Many of these agents are known to produce lesions elsewhere in the central nervous system. Because of its complexities the central auditory mechanism is unexplored from this standpoint and it is not possible to speculate on the importance which vitamins or other factors might have in maintaining its integrity. In other words to credit the changes in the peripheral auditory mechanism produced by these agents with all the impairments of hearing is erroneous. The story is only half told from experimental studies involving the middle and internal ears and the peripheral nerve.

CONCLUSIONS.

1. Vitamin A deficiency in rats is associated with middle ear infections, increase in the periosteal layer of the otic capsule and occasionally exostoses in the internal auditory canal, degeneration of the cells of the stria vascularis, external sulcus cells and parts of the organ of Corti with slight to moderate demyelinization of the cochlear nerve.

2. Vitamin B_1 and various factors of the B_2 complex result in a higher incidence of middle ear infections, when one of them is lacking in the diet of animals. Avitaminoses of the B group cause no significant changes in the bone of the otic capsule or ossicular chain. Degenerative changes are found in the external hair cells of riboflavin deficient animals. Spiral ganglion cells are altered in appearance in all avitaminoses of the B group, less for B_6. Demyelinization of the cochlear nerve, particularly in the dendritic portion, has been found to be more severe for animals maintained on these diets. In fact, the anti-gray hair factor is the only exception. According to the present series the three most important vitamins for the maintenance of the myelin sheath of the nerve are, in order, vitamin B_6, thiamin chloride and riboflavin. Such evidence as we have to date indicates that the cochlear nerve is more susceptible to alterations than the vestibular portion of the VIII Nerve or any other cranial nerve, with the possible exception of the optic. An explanation may be found on the basis of phylogeny, because the cochlear nerve is relatively recent, phylogenetically.

3. Vitamin C deficient guinea pigs reveal hemorrhage into the lining of the middle ear cavity with an increase in thickness of the submucosa. There is a tendency for cellular marrow to be replaced by fibrous marrow. Only slight demyelinization of the cochlear nerve is produced. The cells of the organ of Corti, including the hair cells, are swollen and degenerated, and also some of the cells of the stria vascularis. Chronically deficient vitamin C guinea pigs may reveal more extensive changes, particularly within the ossicular joints and the bone of the capsule. This subject is to be further studied.

4. Vitamin D deficient rats frequently have infections of the middle ear. This deficiency is to be associated with the laying down of osteoid in the bone of the ossicular chain and otic capsule. Demyelinization of the cochlear nerve also accompanies this vitamin-lack. The effects of hypervitaminosis D_2 on the bone of the capsule of young animals is to be reported subsequently.

5. Vitamin E-low rats (third generation) show middle ear infections. The muscles of the middle ear, particularly the tensor tympani, contain considerable fibrous tissue replace-

ment of the muscle bundles. It has been found for other deficiences that the presence of an otitis media may result in atrophic changes within these muscles, because of the penetration of the exudate into the muscle substance and subsequent inflammatory reaction. Small exostoses and irregularities in the periosteal bone are in evidence. Hemorrhages about the nerve in the modiolus, under the dura and submucosa of the middle ear are present in these "E" deficient animals.

REFERENCES.

1. Covell, W. P. and Noble, L.: The Significance of Myelin Sheath Degeneration for the Cochlear Nerve. *Ann. Otol., Rhinol. and Laryngol.*, 46:895-912, 1937.

2. Covell, W. P.: Histopathologic Changes in the Peripheral Auditory Mechanism for Experimental Avitaminoses. Paper presented before The Research Study Club, Los Angeles, California, Jan. 23, 1938.

3. Wolbach, S. B. and Bessey, O. A.: Relative Overgrowth of the Central Nervous System in Vitamin A Deficiency in Young Rats. *Science*, 91:599-600, 1940.

4. Rinehart, J. F.: Studies Relating to Vitamin C Deficiency. *Ann. Int. Med.*, 9:671-689, 1935.

5. Jones, I. H.: Vitamins and the Ear, Nose and Throat. The Laryngoscope, July, 1940.

6. Selfridge, G.: VIII Nerve High Tone Deafness from a Nutritional Standpoint. *Ann. Otol., Rhinol. and Laryngol.*, 46:93-118, 1937.

7. Mellanby, E.: The Experimental Production of Deafness in Young Animals by Diet. *J. Physiol.*, 94:380-398, 1938.

8. Ono, T.: Experimentelle Histopathologische Studie des Gehörorgan bei der B- and C-Avitaminosen. I. Mitteilung. *Trans. Japanese Pathol. Soc.*, 18:172-175, 1928.

9. Loch, W. E.: Veränderungen der Labyrinthkapsel bei tierexperimentellen Avitaminosen (A, C, D, E). *Monatsschr. f. Ohrenhl.*, 73:542-561. 1939.

VITAMIN B AND OTHER MEASURES IN THE TREATMENT OF DEAFNESS.

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A review of the literature on the above subject and considerable experience with it indicates to the writer that treatment of deafness is, on the whole, most unsatisfactory. Types of deafness for which little but moral support can be offered the average patient include otosclerosis, perceptive deafness resulting from trauma, from neurotropic infections and that seen in the elderly patient; also many cases of middle ear deafness, particularly if of long duration, whether the perceptive element is affected or not. A majority of those who are hard-of-hearing may have their hearing impairment classified in one of the above groups, and those who can be helped by treatment form a disappointingly small percentage of the total number of individuals who have defective hearing, which has been estimated as 10 per cent of the population. In deafness as a rule, as in cases of tinnitus, not even symptomatic relief is obtainable, in spite of the many therapeutic measures being employed; and although some of these have been used for years, statistical evidence of their value is difficult to find. Until such statistics are published, enthusiasm over any method of treatment should be balanced by sufficient skepticism. Appreciation of the limitations of hearing aids and of therapeutics in deafness will enable the physician to dispense with useless or harmful measures and to devote his energy to the more important preventive phases.

Thorough periodic examinations, both general and otologic, are desirable, and the latter should include the tuning fork tests as well as the use of the audiometer. A careful history and detailed study of each patient, of his family, of vocational and social adjustments, and any factors with a possible bearing on the hearing helps materially to a better understanding of deafness and is essential if proper advice is to be given concerning training in lip-reading, use of earphones or of various therapeutic measures under consideration.

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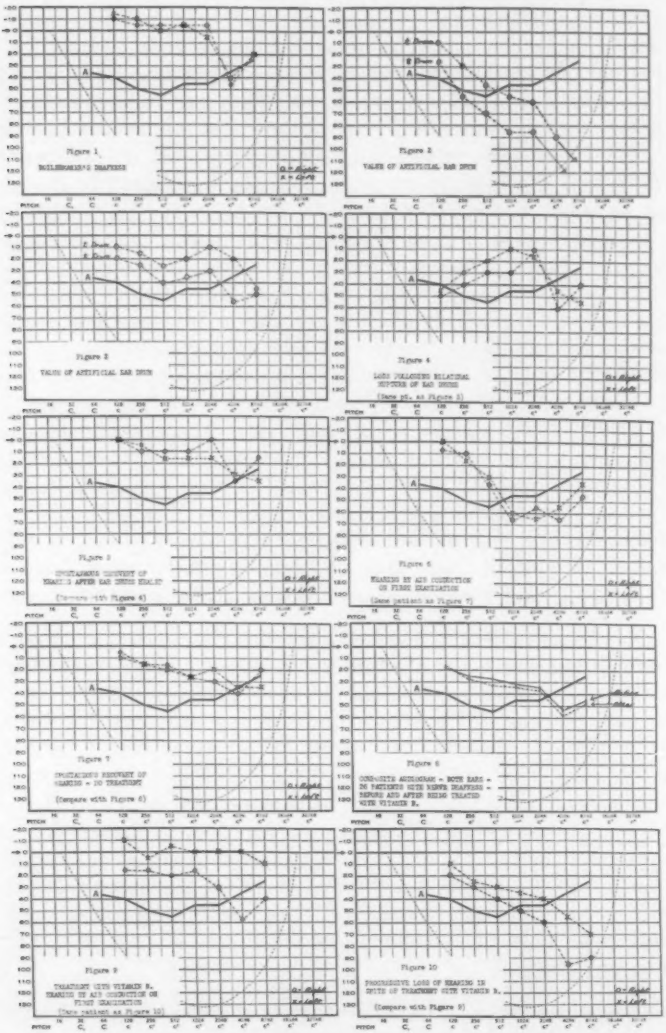
Because hearing aids as a rule are expensive and of limited usefulness, their value should be demonstrated by comparative audiograms before purchase, and a reasonable trial period should be permitted to allow the patient's primary enthusiasm to subside. To obtain the most benefit from them requires patience and re-education on the part of the patient, and it is gratifying to see more hearing aids in use, an indication that those who are hard-of-hearing are, as a group, less sensitive about wearing them. They are indispensable to many with a conduction type of deafness but should be prescribed carefully. Even the best hearing aids do not reproduce well the high frequencies, and the hand held to the ear is as good a resonator as some horns used. In perceptive deafness and in mixed deafness with much impairment of the perceptive element, hearing aids are unsatisfactory. A microtelephone may distort sounds at frequencies other than its own, and valve amplifiers are apt to be less clear as the sound is amplified. Earphones are only mechanical aids to deafness and their inadequacy is illustrated by the fact that patients who use them without some lip-reading are rarely entirely satisfied. Hearing aids are unnecessary to the patients whose hearing is only moderately impaired and to those who have difficulty only with hearing speech at a distance. The electric hearing aid amplifies all sounds without selection, and in a patient with nerve deafness if the amplification is marked there may be head noises, tinnitus, fatigue of hearing and possibly some damage to the auditory nerve.

Deafness following exposure to loud sounds may in time become less marked, as when boilermakers change their occupation to a quiet one. This type of deafness, first characterized by a loss of acuity in the hearing range at 4,096 d.v. (C_5) may be unsuspected unless it is accompanied by tinnitus (see Fig. 1). Fatigue of the auditory nerve is most easily demonstrated in those with some perceptive deafness by reapplying the still-vibrating tuning fork to the ear a few seconds after the patient has said the sound stopped. Almost invariably the sound will be heard again, the nerve having recovered from the fatigue. Patients with perceptive deafness hear best in the mornings when rested both mentally and physically.

It has been shown that the hearing of those with otosclerosis may vary about 10 dcb. Probably those with normal

hearing vary at times in their ability to hear. An improvement of slight degree in the hearing must not be taken too seriously, particularly when such improvement follows some



new method of treatment or is not properly controlled. The audiometer provides a fairly accurate method of charting the condition of the hearing and of evaluating treatment. Immediate improvement in hearing following the use of a hearing aid is illustrated by Figs. 2 and 3, which are the audiograms of the right ear of two patients with conduction deafness, the drums having been destroyed as a result of otitis media. The lower curves were made without a hearing aid; the upper ones were made 10 minutes afterwards, an artificial eardrum having been inserted. Such treatment is palliative only and, unfortunately, few of the methods of treatment result in as much improvement, *per se*.

A recent statement that in an eastern city, of 900 children with defective hearing, approximately 50 per cent had been corrected, sounds too optimistic, because in a group such as that, middle ear deafness would be the predominating type to show improvement, since children with nerve deafness tend not to improve. Even granting that this degree of recovery occurred, one wonders how much of it was spontaneous, rather than the result of treatment. Spontaneous recovery of hearing is illustrated by Figs. 4 and 5. The patient, a machinist, sustained bilateral rupture of the eardrums, the result of an explosion of hydrogen gas. Fig. 4 is the audiogram before, and Fig. 5 after the drums had healed. No treatment was given. Fig. 5, also like Fig. 1, illustrates the residual loss at 4,096 d.v. due to previous injury to the nerve, the result of working in the noise of a machine shop. Figs. 6 and 7 illustrate the spontaneous improvement in hearing occuring in another patient.

It is difficult to understand how some of the various measures used could help certain types of deafness, although understanding can be disregarded if there is truly improvement. Massage of the eardrums, inflations and dilatations of the Eustachian tubes, the latter at times with heated bougies, the use of thyroxin or other medication such as iodine vapor, ephedrine or cocaine in the middle ear or Eustachian tube, the finger in the nasopharynx, ionization, diathermy, the use of respiratory vaccines, thyroid extract, insulin and of Roentgenography of the cervical sympathetic may be mentioned as measures of doubtful value which should not be employed indiscriminately. It seems unreasonable to expect

any such measures to stimulate the hearing apparatus or auditory centre to function better. Some improvement in hearing has been reported in otosclerosis after suboccipital puncture and after thyroxin was administered. It has been said that disorders of the temporomandibular joint may affect the hearing indirectly by keeping the Eustachian tube closed, and correction of malocclusion is recommended as an indirect aid of hearing. This is probaby one of the less likely causes of deafness. It seems reasonable that lymphoid tissue may occlude the Eustachian orifice, causing deafness, and that irradiation may correct this, but in the experience of the writer it is much commoner to find the Eustachian tube occluded as a result of catarrhal inflammation originating in the nose and in the lymphoid tissue of the nasopharynx rather than in lymphoid tissue situated in the Eustachian orifice itself. Nearly every patient who is hard-of-hearing and who has been treated previously states in his history that he has had his Eustachian tubes catheterized, almost invariably without benefit. Even when the feeling of fulness in the ear is relieved by inflations, this relief is usually of short duration, measurable in hours. As pointed out by Friesner and Druss, there is no essential difference between acute catarrhal otitis, suppurative otitis and fibrous adhesive state, all being different stages of the same inflammatory process. Restitution takes place in the majority of the catarrhal stages, while in others scar tissue develops, and it is certain that medical treatment cannot cure fibrous adhesions in the tympanic cavity. Healing in such cases occurs spontaneously, not as a result of futile, though popular, therapeutic measures. The Eustachian catheter can, if used repeatedly or carelessly, result in middle ear disease and should be employed less often. More recently, prostigmin, of so much benefit in myasthenia gravis, has been said to help cases of acute conduction deafness in improving the hearing and in relieving tinnitus. The limited experience of the writer in the use of this substance has failed to demonstrate any benefit in such cases.

When the cause of deafness is discoverable and can be corrected, one may expect partial if not complete recovery, providing the hearing has not been impaired too long. This applies to deafness from some specific diseases, from allergy, drugs, impacted cerumen and from exposure to loud noises.

Unfortunately there is much deafness in healthy people of exemplary habits. They may not use drugs, alcohol or tobacco and give no evidence of harboring remote foci of infection; they are not diabetic; their thyroids function properly; and they have no nasal, sinal or active aural foci of infection.

Nutritional and vitamin therapy of deafness has been studied for some years without it having been shown that deficiency of vitamin A or B caused deafness. At present, vitamin therapy is perhaps being used to excess in many disorders, and deafness is receiving its share of vitamin therapy, for the B-complex is now said to help the perceptive type of deafness. The daily papers are perhaps too quick to report such treatments and the optimistic public too anxious to try them. It is to be hoped that studies on the effect of these substances will be well controlled and that definitely beneficial effects will be shown to occur.

Most nonspecific nerve deafness occurs in elderly individuals of either sex, and the acuity of hearing for the high frequencies in many otherwise healthy persons decreases more or less constantly with each decade after the fourth. Hall has stated that over the age of 65 years entirely normal hearing occurs in only 16.1 per cent of cases. If nerve deafness can be largely explained by a deficiency of vitamin B, it seems that there should be other evidence of such avitaminosis and strange that such a lack would predominate in patients in the older age groups. One suspects that the average adult diet, even in those with nerve deafness, contains an adequate supply of this vitamin which is fairly widely distributed, for, when questioned concerning a list of foods containing this substance, most patients are sure of no lack of it. It is said that saturation with it may be essential to a therapeutic result, although just why is not clear, even though the substance is not stored in the body. It is said, too, that cases of constitutional deafness have been benefited in some instances by the use intranasally of estrogenic substances. Many cases of perception deafness might be classified as constitutional, and it seems as reasonable to expect improvement in these following treatment with glandular extracts, some of which are inert, as after the use of vitamin B-complex, which is readily excreted. One wonders whether some other factor such as heredity, senility or endocrine dis-

orders may not be fully as important in the etiology of perceptive deafness. Although the therapeutic dose, except for experimental animals, has not been established, empiric use of vitamin B may be condoned on the ground that the various components of the complex have been identified relatively recently, and accurate tests for their presence are not yet widely available. Because vitamin B seems harmless and for lack of something better, it has been given by the writer for over a year to many patients with nerve deafness and to those with combined deafness with a large nerve element, no other cause for the hearing impairment being demonstrable. It is hoped that both the dosage and method of administration were inadequate, for very few patients felt that they were benefited, and even these were shown by the audiometer to be no better. Thiamin chloride, as well as the entire vitamin B-complex, were given orally, the dosage varying from 300 international units to 1,200 units daily, and thiamin chloride in 3,000 to 5,000 unit doses was given subcutaneously, the average oral daily dosage being 672 units. The periods of oral treatment varied between two and 46 weeks, and averaged seven and three-tenths weeks. Nearly every patient was given a list of foods rich in vitamin B and advised to use these freely. Audiograms, made after treatment in 26 cases, showed no gain in hearing in any case (see Fig. 8). One woman, age 29 years, had a nonsyphilitic loss of hearing in one ear of only a few months' duration (see Fig. 9), and the hearing in the other ear was normal. After taking vitamin B for seven weeks the loss in the right ear had increased, and in the left ear the hearing was also much impaired (see Fig. 10).

Thiamin chloride was used in many cases of tinnitus but in only one did it appear to give relief. In this case, a woman in the menopause with intractable and severe tinnitus and hyperacusis, received by subcutaneous injection 10 mg. of thiamin chloride (3,000 units) on two occasions and on alternate days, and was relieved quickly and completely of both symptoms for two and one-half months. When the tinnitus recurred, three more injections were given within five days and this time the symptoms were relieved for four and one-half months. In this case no previous treatments had been of benefit, and these included inflations and bouginage of the Eustachian tubes, the use of novocain intravenously, of ammonium chloride and Furstenberg's diet, of myringotomy

and of various sedative drugs. The medical treatment of tinnitus is even more unsatisfactory than that of deafness, unless the cause is some focus of infection, or a drug or poison which may be eliminated. In only one out of many cases of tinnitus did the use of an estrogenic substance seem to help.

In toxic nerve deafness the elimination treatment consisting of daily sweating with pilocarpine, 0.01-0.02 gm., the use of a quart of hot tea, and rubber sheets, prohibition of tobacco, alcohol, certain drugs and the restriction of fluids should be tried. This type of treatment and Furstenberg's treatment might conceivably help those hard-of-hearing as a result of an exudative labyrinthitis, whether of allergic, toxic or other origin, assuming the pathology to be edema of the inner ear, or be of benefit in secretory otitic or conduction deafness, in which more or less the same process occurs in the middle ear.

Although the operations of Sourdille and Holmgren for otosclerosis, in which a window is made into the labyrinth, may in time be perfected sufficiently so that the initial improvement in hearing persists indefinitely, and although Holmgren has reported 100 operations without complications, yet these operations are still in the experimental stage and should only be done by experts and with a clear realization on the part of both physician and patient of the probable outcome. To be suitable for such an operation, the tympanum must be free of infection, the stapes anklyosed, and an appreciable perceptive element be retained. If a successful result depends on obtaining a permanent fistula of the labyrinth, and if such a fistula is as difficult for the average specialist to obtain as is a permanent window in the maxillary antrum, then no doubt it will be some years before much help can be hoped for from this operation, for intranasal operations on the antrum described over 30 years ago have not as yet enjoyed the popularity they merit.

Preventive measures are at present more important than any other type of therapy and vary with the various types of deafness. Those whose occupations expose them to loud noises should protect the ears by plugging; those with otosclerosis should be advised of the hereditary factor and warned of the possibilities of transmitting the defect to their descendants;

the high-strung, nervous, worrying type of individual who ages too rapidly must be encouraged to take life easier, to avoid unnecessary responsibilities and fatigue, both physical and mental, and thus postpone as much as possible the onset of senility and of senile nerve deafness. That large groups of persons afflicted with catarrhal deafness should be reduced by attention to disease of the nasopharynx and sinuses, whether allergic or infectious, to nasal obstruction, septal spurs, to the avoidance of forceful and improper nasal douches, nose-blowing and swimming. There often seems to be a relation between the side of the nose affected by obstruction or disease and the ear that is hard-of-hearing. Where the climatic factor predisposes to respiratory and aural infections which occur in spite of various remedies, the patient should be advised to change his residence if possible. No doubt the removal of tonsils and adenoids in childhood, and even in infancy, is one of the greatest single measures towards prevention of middle ear disease and of conduction deafness and should be encouraged by general physicians, pediatricians and obstetricians. Otorrhea, which is often of nasal or sinal origin, may, as in a Type I ear, depend almost entirely on the nose. When the aural discharge continues in spite of treatment and results from disease in the middle ear or in the mastoid antrum, appropriate surgery should be done unhesitatingly. Attention to the general health, that is, co-operation between the otologist and internist, is important; foci of infection should be eliminated and faulty habits of breathing, eating, working and living in general should be corrected. Many patients, in spite of having received no benefit from treatment, persist in hoping for relief from the hearing impairment. They prefer to believe their condition to be curable, fear a frank opinion and wish reassurance. It may be wiser not to attempt to dispel suddenly their hopes. One may be justified in using upon such a patient any new remedy which promises some help, provided it is not harmful, even if it is only to convince the patient that nothing is to be gained from further treatment. Some patients, particularly those with nerve deafness in the older age group, will be satisfied if they can be told that their hearing is as good or better than the average for a patient of their age, and others with a conduction type of deafness may be satisfied if they are reassured that they will not become entirely deafened.

Even those whose hearing is not improved by treatment may derive considerable satisfaction from the interest taken in them, the art of medicine in such cases being more valuable than the science. Impaired hearing is a tragic thing to many who require moral support, while others accept it placidly and soon adjust themselves to their new state. Considerable persuasion may be necessary to have a sensitive patient use an earphone, and others, easily discouraged, will not persist in the study of lip-reading.

Although the loss of hearing today is a greater handicap than in former years, deafness is rarely complete, and with proper preventive measures will become less common. Even a little hearing often is of considerable benefit to the proficiency in speech.

BIBLIOGRAPHY.

FRIESNER, I., and DRUSS, J. G.: Critique of the Present Treatment of Deafness Due to Lesions in the Conduction Mechanism. *Arch. Otolaryngol.*, 26:259-269, Sept., 1937.

HALL, J.: The Hearing Study Series of the National Health Survey. *Amer. Jour. Deaf.*, 83:457-460, Nov., 1938.

Greens' Eye Hospital.

THE RECOGNITION, TREATMENT AND PREVENTION OF HEARING IMPAIRMENT IN CHILDREN.*†‡

DR. S. J. CROWE, Baltimore.

I speak for the entire Baltimore group when I say it is a great pleasure to present to you a summary of our work on the ear. It is distinctly a group study, and many whose names are not on the program have contributed as much as those of us who are reading the papers here this morning.

I wish to make it very clear that we do not advocate the indiscriminate use of radium as a treatment for deafness. It may or may not improve the hearing in a given case, depending on the cause and duration of the impairment. Radium is of great vaue in re-establishing the lumen and the function of a Eustachian tube partially occluded by hyperplastic lymphoid tissue. In other words, it is used to correct a condition that predisposes to impaired hearing and attacks of otitis media. The best results are obtained when it is used in children with beginning impairment of hearing. Only rarely are spectacular results obtained in extremely deaf children or in adults.

The studies on school children reported in the papers which follow are not completed; they are a preliminary report of work in progress. About 700 of these children must be re-examined from time to time during the next five or 10 years before we can answer many of the questions you will doubtless ask, such as, in what percentage does Eustachian tube obstruction in childhood and the resultant partial deafness for high tones progress to a more severe and permanent deafness later in life?

We are not comparing the various methods for treating impaired hearing in children, or insisting that radium is bet-

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ter than other agents, but pointing out that in our experience radium is an effective, safe and painless method of reducing lymphoid tissue in and around the Eustachian tubes that cannot be removed surgically.

We have been studying intensively for 16 years the causes, the pathology, treatment and possible methods for the prevention of deafness. For the first 14 years we used the method that has been employed so successfully in studying the diseases of the heart, lungs, kidneys and other parts of the body — *i.e.*, the correlation of the clinical examinations and functional tests with the gross and histologic appearance of the organ after death. This method has its shortcomings when a special sense organ like the ear is being studied. We have learned much about the pathology and the interpretation of hearing tests but very little about where the lesion began, the early symptoms, the primary cause of the trouble, how it progressed, how rapid was the progression, and other facts that are essential before effective methods of treatment or prevention can be devised.

During the past 16 years we have made, for research purposes, audiometer, tuning fork and voice tests on more than 15,000 patients, approximately 3,000 of whom were children. These tests were all made in a soundproof room with the 1A Western Electric audiometer with a range of from 32 to 16,384 d.v.

As the years passed, we have become more and more convinced that many of the hearing disorders of adult life begin in childhood, and if we are to learn more about the causes, treatment and prevention of deafness we must concentrate our studies on children.

From the studies made on children so far we have learned: that adenoids recur in more than 75 per cent of the children whose tonsils and adenoids have been removed before the age of puberty, and that the recurrence in the nasopharynx often interferes with the ventilating function of the Eustachian tubes and leads to an insidious, painless type of progressive deafness. The explanation for the recurrence of lymphoid nodules in the oro- and nasopharynx is that lymphoid tissue is an integral part of the mucous membrane in this area, and it is impossible to remove all of it at operation. It is not the

size but the location of the lymphoid tissue that impairs the hearing. The treatment is not a second operation, but radiation.

In some children the growth of lymphoid tissue is excessive, in others it is very slight. If we understood better the basic problem of why some children are more susceptible to respiratory infections than others; if we knew what is the relation between dietary deficiencies, ductless gland disorders and lymphoid hyperplasia it would probably not be necessary to operate, radiate or treat the symptoms of lymphoid hyperplasia in any way. The cause could be corrected at the source.

We have also learned that almost every type of middle and inner ear deafness seen in adults is also found in children from 8 to 14 years of age. There is this important difference, however: In children, the impairment of hearing is just beginning, and better opportunities are offered for study of the life history of the disease and its complications, and for instituting some kind of effective or preventive therapy. In most adults the malady has been in the making for many years, and the hearing apparatus is irreparably damaged. There is so little chance that we will ever be able to cure deafness in the adult that we must seek for a clear understanding of the causes and methods of prevention in children.

In childhood, when the hearing impairment is just beginning, all types of middle and inner ear lesions, with the possible exception of otosclerosis, have one symptom in common; *i.e.*, the hearing is more impaired for high than for low tones. It is certain that we must revise our ideas about the diagnostic significance of audiometric tests in children that show more impairment for high than for low tones. This finding does not always indicate an inner ear or nerve lesion, even if the hearing by bone conduction is also much impaired.

We know that an overgrowth of lymphoid tissue which partially obstructs the Eustachian tubes for a period of years causes changes in the mucous membrane of the middle ear. At first it is hyperemic, then passes into the secretory stage, gradually becomes myxomatous and, finally, fibrous tissue is formed which interferes more and more with the mobility of the ossicles. These changes are very prone to occur in the attic, and on otoscopic examination the first changes to be

seen in the tympanic membrane are usually in Shrapnell's membrane.

We have learned that impaired hearing in children, whatever the primary cause, is almost invariably complicated to a greater or less degree by partial Eustachian tube obstruction, secondary to hypertrophied lymphoid tissue in the nasopharynx.

The patency of the Eustachian tubes in children is not determined by inflation, which is a very artificial procedure, but by three procedures: *1.* Inspection of the tympanic membranes for retraction (especially in Shrapnell's membrane); *2.* the examination of the nasopharynx with a nasopharyngoscope (which, under local anesthesia, is just as simple in children as in adults); *3.* a voice test with the opposite ear masked, and an audiometric test with particular reference to 8,000 d.v. and the higher tones.

Regardless of the primary cause of the deafness, every child with evidence of Eustachian tube obstruction should have something done to restore and maintain its patency. This is particularly important in children with some residual hearing who are being trained in schools (like Central Institute for the Deaf) to use to the best advantage any hearing they may have.

In conclusion, I wish to stress five points:

1. The recurrence of adenoids after operation on young children is so common that it must be regarded as normal.

2. This recurrent lymphoid tissue may impair the function of the Eustachian tubes and cause a low grade tubotympanic catarrh, which may lead to chronic progressive deafness.

3. Recurrent or hyperplastic nodules of adenoid tissue in and around the pharyngeal orifice of the Eustachian tubes are so located that they cannot be removed surgically.

4. Lymphoid tissue is so sensitive to radiation that the dosage employed in the treatment of the nasopharynx is far below the amount that could cause any irritation or injury to the mucous membrane or surrounding structures. No scar tissue, no dryness of the nose or throat, and no atrophic

changes in the nasal mucosa follow treatment of the nasopharynx with radon, provided the proper dosage is given at the proper intervals. This statement is based on our observation of hundreds of children. Many of them have been followed for 10 years or more. If used carelessly or if the treatments are intrusted to a technician, radium therapy may be extremely dangerous. It should never be given in the presence of an acute nasopharyngitis. The object of the treatment is to reduce the size of lymphoid tissue. It has little or no direct action on bacteria.

5. Radiation is of no value in the treatment of chronic middle ear suppuration, otosclerosis or any form of inner ear or nerve deafness. It is used for the sole purpose of reducing obstructing nodules of lymphoid tissue, decreasing the secretion of mucus and restoring the normal ventilating function of the Eustachian tubes. For this reason radiation is more often beneficial in children than in adults. To obtain the best results it must be used before changes in the middle and inner ear, secondary to partial tubal obstruction, have irreparably damaged the middle and inner ear structures.

Johns Hopkins University.

IRRADIATION TREATMENT OF HYPERPLASTIC LYMPHOID TISSUE.*

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My interest in the subject of this symposium is entirely due to a long and instructive association with Dr. Crowe. It began nearly 20 years ago with the planning and carrying out of various methods of irradiation in treating nasopharyngeal neoplasms. As early as 1926, an applicator, essentially identical with that now employed, had been developed and has been used ever since for various purposes.

As I understand the problem, surgical adenectomies, under the very best technical conditions, leave something to be desired in the matter of preventing deafness in children due to Eustachian tube obstructions. In addition to the possibility of improving results by irradiation, it was hoped that a simpler, more economical and, consequently, more widely usable method might be developed.

The reason for believing that irradiation might be suitable for this purpose rests on both experimental and clinical observations, indicating that lymphocytes and lymphatic tissues are much less tolerant to raying than the other tissues met with in the nasopharynx. Ray tolerance, or ray sensitivity, are terms frequently employed in radiological literature; they express inverse relations — low tolerance means high sensitivity and vice versa, high tolerance indicates low sensitivity. A sensitive tissue can be described as one which is severely changed both macro- and microscopically by doses of irradiation which produce little or no change in surrounding tissues. It is obvious that the entire rationale of irradiation therapy rests on such differences in tissues, normal and pathological. As early as 1904, Heinicke experimentally demonstrated that lymphocytic tissues are very radiosensitive. His experiments have been frequently substantiated, and clinically they have been confirmed by the effects produced on lymphosarcomas, lymphoblastomas, lymphatic leukemias

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and in hyperplasias of the thymus gland, lymph glands, tonsils and other conditions.

It should be kept in mind that irradiation, even when no visible effect is observable, is probably always an injurious agent. The less the injury to any living tissue, the more rapid and complete the recovery. A corollary to this statement is that the ideal application of irradiation is one in which the pathological volume receives all the treatment, and other tissues none. This ideal can never be attained, but the nearer it is approached the better will be the result to be expected. This phase of the matter will be referred to a little later in describing dosage.

Perhaps a few general statements which fairly well represent current opinion regarding irradiation will not be out of place.

The most vulnerable part of the cell is the nucleus. A dividing cell is more sensitive than the same cell in other phases of its life. The reproductive elements of cells are less tolerant than the vegetative parts. The actual colloidal condition, which varies continuously, is a determining factor. The surroundings and nutrition are very influential in determining sensitivity. Infection alters conditions markedly. The irradiation absorbed in the tissue, and not that which passes through unchanged, is the effectual factor. Providing absorption of energy is equal, no great nor definite differences between different types of irradiation have been established.

There is no definite knowledge as to why one cell or one tissue is more radiosensitive than another. This applies to different varieties of flies, objects much used in genetic studies, as well as tissues. Some day in the future is reserved for a clearing up of the physical and biochemical processes involved in irradiation. Fortunately, as far as our problem is concerned. these problems do not have to be solved in order to intelligently employ irradiation for adenoids and deafness.

In planning a method of irradiation suitable for children, several considerations must be kept in mind. The first of these, of course, is that the procedure be adequate in reducing or removing the offending adenoids, and relieving or improving the impairment of hearing. The second, equally as impor-

tant, is that no injury be done to the nasopharynx or to the child by the treatment. Of less importance, but nevertheless to be considered, are such factors as expense in money and time, comfort of the patient, ease of employment by the doctor giving the treatment, and a technique where the chances of error are reduced to a minimum.

Two available procedures came to mind at once as suitable for our purposes: *1.* the placement of the source of radiation directly in the nasopharynx — radium or its decomposition product, radon, could be conveniently used in this way; *2.* radiation from the surface or through the mouth with Roentgen rays. The second method has the advantage of

Fig. 1. Nasal applicator: (a) Applicator disassembled. Left to right: handle, glass tube containing radon, brass tube for holding radon, to be screwed on handle. (b) Applicator assembled. Actual length overall, 15 cm.

permitting a more homogeneous dosage to the entire nasopharynx and can take in the entire Eustachian tubes, which is not possible with intranasopharyngeal applications; however, it seems that most of the obstructions due to lymphoid hyperplasia are in the nasopharynx and the adjacent areas of the Eustachian tubes.

From most other standpoints, the intranasopharyngeal procedure is decidedly superior. It is certainly safer and, in fact, seems a perfectly harmless procedure. The absorbed radiant energy is largely limited to the nasopharynx, while surrounding tissues receive only homeopathic dosage. The reverse is true where X-ray is employed. A great deal more radiation is absorbed in tissues which receive treatment given only to reach the nasopharynx. Where X-raying is employed, it should always be through small portals, not over 4 cm. square on the surface. In this way, it is possible to reduce the absorption in normal tissues to a minimum. We do not know enough

about the possible late injuries of growing bones, glands and other structures in children which might result from this kind of treatment. Done very carefully, there is, in all likelihood, no injury; but, after all, we are not treating malignant tumors and even a very small percentage of injuries would invalidate a method of treatment.

You may wonder why irradiation from the nasopharynx leads to such a minimal dosage on the normal tissues of the head. The explanation is simple. The intensity and the time of radiation determines the dosage. The intensity varies inversely with the square of the distance of the object irradiated from the source of irradiation. To give an example: If a determined dosage from a given source of radiation is obtained in a unit of time at 1 cm. distance, at 2 cm. distance, only one-fourth of such a dosage is obtained, and at 3 cm. only one-ninth.

With young children, where small portals of X-ray are used, there is also the problem of keeping them still so that accurate crossfiring can be carried out. There is a considerable risk of getting the beam out of line, and it is always hard on the child. If one employed large portals from either side of the head, it would be very easy to give the necessary dosage to almost any child, but under such conditions there is entirely too much treatment given to the head in proportion to that which is received by the nasopharynx. The cost involved in giving X-ray treatments is certainly much greater than that which is entailed by using the radium or radon in the nasopharynx. It would be difficult for an otologist to carry out such treatment in his office or in a hospital; in fact, I feel that such treatments should only be carried out by a person who has been thoroughly trained in giving X-ray exposures. It is perfectly possible for the otologist who is studying the child, both by hearing tests and by examinations of the nasopharynx, to employ the intranasopharyngeal treatment with radium or radon. Personally, I feel this is a great advantage in the individual case, and also will lead to a more thorough development of the technique and avoidance of all complications.

Having given the reasons for our preference to radon and radium over X-ray, there remains to be said a few facts about these elements. The quality of radiation from radon and

radium is exactly the same. The rays in each case come from decomposition products known as radium B and C. In the course of their decomposition, substances which do not give off rays are produced. When a radium salt such as sulphate or chloride is sealed in a glass tube or other container, it begins to undergo a slow decomposition and liberates a gas. This gas is called radon. Neither the radium nor the radon give off, as stated, any rays. The first decomposition product from radon is radium A, and from this comes radium B, and from this, radium C. It takes about 30 days for radium sealed in a glass container to reach a stage of equilibrium — that is, the stage in which the amount of radon, radium B and C, are constant. A given amount of radium liberates about one-sixth of the total amount of radon which exists when full equilibrium is established in 24 hours. When radium is kept in an aqueous solution, it is possible to separate the radon and put it into a sealed container. It reaches its stable equilibrium in about three and one-half hours, and then begins declining in an exponential fashion, reaching half value in three and eight-tenths days. It is obvious from what has been said that with a radium container the amount of radiation is always the same; where radon is employed, one has to have tables showing the strength at any given moment. In this way the radium has an advantage over the radon. It also, of course, has the advantage that it does not have to be constantly renewed. Its disadvantages are that the applicators are a great deal weaker, as much more radon can be placed in a given volume than radium; also, one is freed from the fear of loss by breakage, theft or accident, and the problem of adequate sterilization is a little simpler.

In an applicator which I am going to describe, it is easily possible to put 1,000 millicuries of radon or more, if one has the supply of radium for such amounts. I am advised that in an applicator of the dimensions which we use, approximately 50 mg. of pure anhydrous radium sulphate can be placed. It is also possible, of course, to have two such applicators made and use them both at the same time.

Dosage: As already stated, with an applicator containing a given amount of radium or radon, the dosage, which is a product of the quantity and the time involved, is easily obtained by simple division. If it is desired to give 2,000 mg.

minutes and the applicator contains 50 mg., one has only to divide 50 into 2,000, which gives 40 minutes, the time of the dosage. We prefer our notations in gram minutes to milligram minutes, as it involves smaller figures and also allows for greater variations in accuracy. We have used the terms "milligram" and "millicurie." Milligram is the term employed when radium is used, and millicurie when radon is the source of radiation. A millicurie is the amount of radon which exists in equilibrium with a milligram of radium.

The Applicator: It is very inconvenient and, indeed, impossible in children to place applicators in the nasopharynx by going through the mouth and behind and above the soft palate. It would require a general anesthetic in most cases. The applicator should be such that it can be introduced through the nostrils. I understand from Dr. Crowe and his associates, and my own experience bears this out, that the present applicator is small enough even for little infants. It would not be a difficult matter, of course, to make a smaller applicator with the same wall thickness, if this were necessary.

The applicator is introduced along the floor of the nose and carried back to the nasopharyngeal wall. The active part of the applicator is a small glass tube, which is so placed that it does not come in direct contact with the nasal mucosa. The aim is to divide the nasopharynx into two halves, which we can consider as rough spheroids. During the treatment, the applicator should be placed so that the source of radiation is as near the center of the spheroid as possible. If the applicator is introduced through the right nostril, the handle should be drawn over to the left side by a little adhesive passing from the handle to the left cheek and vice versa. The applicator itself is 13 cm. long. The external metal tube into which the handle screws is 2 cm. long. The small glass tube containing the radon is from 1 to 1.5 cm. long. The wall thickness of the metal tube is 1 mm. of brass, and its lumen 1.5 mm. in diameter. The brass applicator looks better if it is chromium-plated. It is well shown in the slide which I present. I also have brought along an empty applicator which will give a better conception of the actual size. Through the walls of this applicator come both gamma and beta rays. The gamma radiation constitutes 95.5 per cent of the total radiation emitted through both the glass and

metal container; the beta radiation, 4.5 per cent. A millimetre of platinum removes all the beta radiation, but there remains a hard secondary radiation from the platinum. There is very little secondary radiation from brass. There is no objection, of course, to using silver, platinum, gold or any other type of screening. The whole purpose of the screening is to reduce the beta radiation. The hard beta rays which go through a millimetre of brass have a penetration in tissue of only about 8 or 9 mm. They are all absorbed in this amount of tissue. The gamma rays, of course, are absorbed to a very much less extent.

It is not, it seems to me, worth while to convert into rs* the amount of radiation which the nasopharynx receives in an intranasopharyngeal application. The chances of error are very great because of variations in the sizes of the nasopharynx. It would, of course, be possible to measure accurately each nasopharynx and calculate the dosage in rs received. If we assume that the spheroid comprising one-half of the nasopharynx has a diameter of 2 cm., and the radium is in the center, the dosage at a distance of 1 cm. would be about 500 rs. The erythema dosage from the radium in a single dose such as we give is about 1,400 rs. Where both sides of the nasopharynx are treated and where the size of the nasopharynx is as indicated, approximately 600 to 650 rs are given. As a rule, we have treated both sides of the nasopharynx at the same treatment. Our average dosage has been 2 gm. minutes. This seems to be a perfectly safe dosage with the applicator we are employing. Not only on account of the adenoids but on account of the normal mucosa, it seems to me that at least six weeks ought to intervene between applications where this dosage is used. This is to avoid any summation of treatment and to allow complete recovery of all the tissues. There is no question in my mind that there is a great variation in the vulnerability of normal hyperplastic lymphoid tissue. As has already been stated, this may be due to differences in vascularization, differences in the rapidity of growth of adenoid tissue, different amounts of edema, and the natural resistance of the patient. Whatever it is, I do not think one can count on exactly similar shrinkage and similar effects in every case. The treatment as a rule causes no reaction or discomfort of any kind immediately or thereafter. The repeti-

*An r is the accepted international unit of Roentgen ray dosage.

tion of the treatment and the number of repetitions should be decided upon the basis of what is found by nasopharyngeal inspections and audiometer tests. It would seem to me that if the hearing has been restored and the Eustachian tube regions are quite clear, that it would be unnecessary to radiate until every bit of lymphoid tissue has disappeared from the nasopharynx. This, however, is a matter for the clinical otologist to determine, and I must confess that I personally do not know whether or not this belief is well founded.

I hope I have presented this problem clearly, and do not feel that any further conclusions are perhaps necessary.

1418 Eutaw Place.

WINNER OF THE 1940 MISSISSIPPI VALLEY MEDICAL SOCIETY CONTEST ANNOUNCED.

The third annual essay contest of the Mississippi Valley Medical Society "for the best unpublished essay on a subject of practical and applicable value to the general practitioner of medicine" has been concluded. The Annual Awards Committee of the Society has announced that Dr. John F. Casey, of Boston, Visiting Physician, St. Elizabeth's Hospital, Boston, is the winner; Dr. F. Stanley Morest, of Kansas City, Mo., second; and Dr. Charles W. Pavey, of Columbus, Ohio, third. The winner receives a $100.00 cash prize, a gold medal, a certificate award, and an invitation to present his essay before the annual meeting of the Mississippi Valley Medical Society. Certificates of merit will be given to Dr. Morest and Dr. Pavey. Dr. Casey will address the Society on the subject of his winning essay, "A Study of the Use of Sulfapyridine and Sulfathiazole in Pneumonia with Particular Reference to the Treatment of Pneumonia by the General Practitioner," at Rock Island, Ill., Sept. 26. The M. V. M. S. Essay Contest has now been established as an annual affair, but the rules for the 1941 contest will not be available until Dec. 1.

HISTOLOGIC STUDIES OF THE EUSTACHIAN TUBE OF INDIVIDUALS WITH GOOD HEARING.*†

DR. LEROY POLVOGT and DR. DUDLEY C. BABB, Baltimore.

There is marked deviation in the histologic structure of the Eustachian tube in individuals with good hearing. The tunica propria is relatively thick in the pharyngeal portion, but thins out toward the middle ear. In the cartilaginous portion of the tube the tunica propria contains many mucous glands (see Fig. 1). The extension and number of glands varies tremendously in different individuals. In general, they extend up further on the medial than the lateral wall. These glands open directly into the lumen of the tube.

A rather striking finding is the varying degree of vascularity of the tunica propria. This vascularity is usually greater in children than adults, but it varies in individuals of the same age group.

The Eustachian tube is lined with ciliated epithelium. The amount of ciliated epithelium found in different tubes is exceedingly variable. It is always found in the pharyngeal end, and frequently extends into the middle ear. It is more often lacking on the lateral wall of the tube than on the medial wall. Interspersed between the ciliated cells are goblet cells. Large numbers of goblet cells are present in some tubes, while in others there are only a few.

The tube may have the appearance of a straight, smooth-walled structure throughout. More commonly, the wall has a corrugated appearance due to evaginations of the tunica propria and epithelium into the lumen (see Figs. 2 and 3). These evaginations may appear as simple finger-like projections, or they may form more complex longitudinal folds. They are more often found in the pharyngeal end, and sometimes exist only in this region. On the other hand, they may extend throughout the entire length of the tube. All variations of these two conditions are found in the tubes studied.

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†From the Otological Research Laboratory, The Johns Hopkins University.

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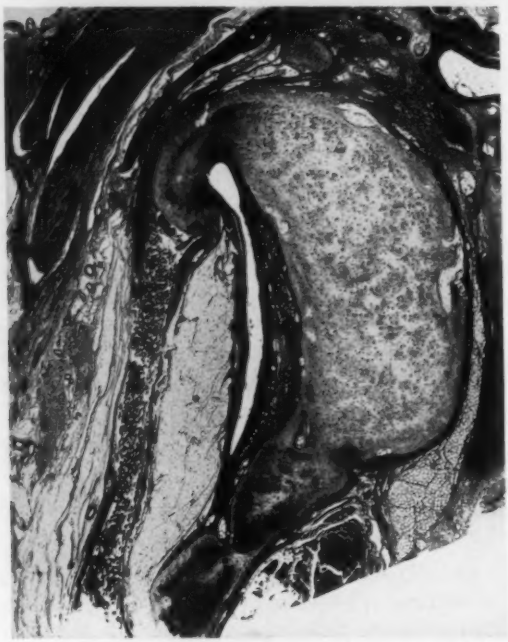

Fig. 1. Section through cartilaginous portion of Eustachian tube.

Fig. 2. Section through junction of cartilaginous and osseous portion of Eustachian tube.

These evaginations frequently contain quite large blood vessels and sometimes lymphoid nodules (see Figs. 3, 4 and 5).

Fig. 3. Osseous portion showing evaginations of tunica propria and lymphoid nodule in tunica propria.

Fig. 4. Osseous portion showing lymphoid nodule and connection with peritubal cell.

The appearance of the tube in its bony portion may be that of a cylinder running through solid bone with little surrounding pneumatization (see Fig. 7), or, due to marked pneumatization, there may be many tubal cells, lined with ciliated epithelium, which are continuous with the main por-

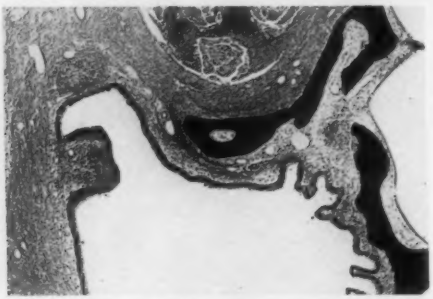

Fig. 5. High power of lymphoid nodule in Fig. 4.

Fig. 6. Osseous portion showing connection with peritubal cell.

tion of the tube and have all the characteristics of the Eustachian tube previously described (see Figs. 4 and 6). In such cases, dilatation of the tube with a bougie may be very difficult and hazardous. Tubal cells allow an easy pathway for the spread of infection throughout the temporal bone.

The most important observation in our studies of these tubes from people with normal hearing is the finding of lymphoid tissue in the tubes. Lymphoid nodules in the tunica propria of the pharyngeal end are rather commonly found. These nodules are observed in all parts of the tube. They may be found deep in the tunica propria or on the surface of

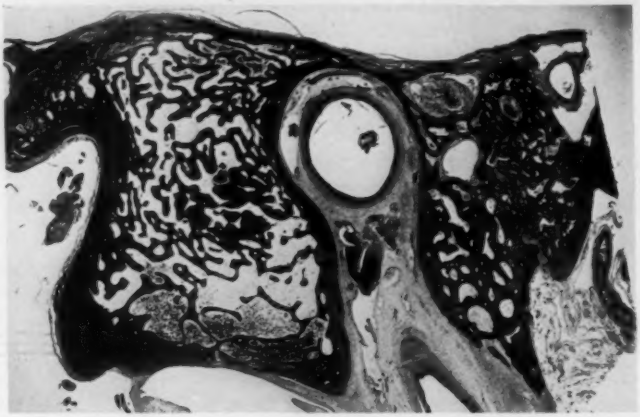

Fig. 7. Osseous portion of Eustachian tube in nonpneumatized petrous apex.

the lining membrane. This tissue is found even in late adult life. It existed in one patient, age 65 years, although it is more frequently seen in young individuals.

The part this tissue plays in impairment of hearing, we have not yet been able to observe. This study includes only Eustachian tubes from individuals with normal hearing. As a result of the present program in the study of the prevention of deafness, we hope to be able to study the Eustachian tubes of those who are known to have had large amounts of lymphoid tissue around the pharyngeal opening of the tubes.

The Johns Hopkins Hospital.

APPLIED BIOCHEMISTRY IN THE ETIOLOGY AND TREATMENT OF SEASONAL HAY FEVER.*

DR. D. C. JARVIS, Barre, Vt.

When contacting an allergic patient the first object of the examination is to learn his racial pattern; the second object is to learn the family pattern he represents; the third object is to learn the distribution of the blood mass in the body, whether in the peripheral vascular bed or the splanchnic vascular bed; the fourth object is to determine whether an oxygen want is present in the tissues supplied by the peripheral vascular bed or the splanchnic vascular bed.

RACIAL PATTERN.

It is possible to determine from physical characteristics the racial strains predominant in the individual and hence be able to state with some degree of accuracy the nutritional requirements of that individual. We can do this in the same way that we can with plants. When we see a plant with certain characteristics we can say, for instance, that this plant is a cactus that has developed through countless generations, is immune to heat, has the ability to conserve moisture, and that it will thrive best under just such conditions as its ancestors learned to combat and to use. Yet these conditions might be very unsatisfactory for a tomato plant or for water cress.

The three white racial strains of Europe are the Nordic, Alpine and Mediterranean. The Nordics lived in coastal regions in the north of Europe which did not support vegetation for several months of the year; therefore, they were largely fish eaters, eating about 10 times as much fish as meat. For vegetation such as is commonly land-grown they depended to a great extent on seaweed washed up on the shore and moss gathered from rocks along the seacoast. Most people of the British Isles are Nordics.

The Alpines, in Central Europe, lived largely on meat, which they gathered from game or from flocks and herds, and upon grain and fruits in season.

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The Mediterraneans, living in a more favored climate than the others, used all classes of foods: sea food, meats, dairy products, grains and fruits.

These racial strains are characterized by the color of their hair and eyes, and the shape of their heads. Those with Nordic characteristics have blue, gray or green eyes, blond or light brown hair, and long heads. The Alpines are characterized by brown eyes, brown hair and round heads. The Mediterraneans have dark eyes, dark hair and long heads.

It must be remembered that a great change has taken place in recent times in the dietary habits of nearly all peoples. With the development of machinery and transportation it became possible to multiply a thousandfold the land under cultivation and hence increased enormously the available food supply.

This in turn allowed a greatly increased population, which increased the more rapidly because of advances made in the control of epidemic disease. It also changed the character of the food from protein to carbohydrate, and from sea food to land-grown food.

This was practically no change at all for the people of Mediterranean descent, and not so much of a change for those of Alpine descent, but was drastic for those of Nordic descent.

Today the United States, the mixing bowl of Europe, offers an unexcelled laboratory for the study of the effects of this changed mode of living upon descendants of these different racial strains. Most of our patients are Nordics. What was formerly considered the strongest and most aggressive strain has become the most vulnerable.

TYPE OF HEAD.

Having noted the color of hair and the color of eyes, attention is next turned to the type of head the patient presents, whether round, medium or long.

The white race has always lived in the temperate or frigid zone and has become acclimated to the conditions found there, and because of the more bountiful food supply and easy means of transportation available has always lived near the

sea. A certain percentage also lived inland and their descendants still do. These people are characterized invariably by round heads, while the coastal people have long or oval heads. There is a great deal of evidence that this round-headed condition is due to lack of minerals in their diet over a long period of time. These people have partially acclimated themselves to the lack of these minerals and as a result suffer less from this lack than people whose ancestry were accustomed to minerals in their diet.

The long heads through the ages have lived on sea food, while the round heads have lived inland. Now nearly all of the so-called civilized peoples of the earth live on land-grown food for the most part. This affects the round heads only to the degree in which their food has been refined, and it becomes a fairly simple matter to enable them to live normally by dietary correction. With the long heads, the case is different. They were mainly protein eaters and sea food was the staple of their diet. It is a great change for them not only to be deprived of the sea minerals upon which they learned to thrive and upon which they depend to a much greater degree than the round heads, but they also are subject to the same changes which affect the round heads.

All animals, including man, have the power of adapting themselves to the conditions which surround them. This adaptation is not accomplished in one or two generations, or several. Many generations are required to even partially secure this result. We, being mostly long-headed people, have not had that background and, therefore, suffer to a greater extent from this mineral deficiency.

Under racial pattern, data is gathered relating to color of hair and eyes; whether the head is round, medium or long; and the place of birth and ancestry of the father and mother, because this information enables one to determine the racial strain predominant in the individual and hence be able to state with some degree of accuracy the nutritional requirements of that individual.

FAMILY PATTERN.

Estimating the family pattern the individual represents, attention turns to a study of the mucous membrane color

within the nose. There are three places in the nose where mucous membrane color is studied: The first is the cartilaginous portion of the nasal septum which is usually available for inspection; the second is the inferior turbinate, which is likewise available for inspection to a greater or less degree; the third is the bony portion of the nasal septum which is not always readily seen, but when seen should be carefully studied. In order to classify intranasal mucous membrane as being red when estimating the family pattern, it should be red in all three locations. If it is pale in one of these three locations then intranasal mucous membrane is classified as being on the pale side. Always study the mucous membrane of the gums, especially the gums of the upper front teeth and the soft palate, as a check on observations made in the nose.

TEMPERATURE.

Continuing estimation of the individual's family pattern, one's attention next turns to the temperature reading by mouth. With 98.6° representing the theoretical normal, one generally finds that patients showing an increased redness of the mucous membrane generally have a temperature two or more tenths above normal, while patients showing a pale mucous membrane generally have a temperature one or more fifths below normal. When taking the patient's temperature no special attention is paid to the time of day it is taken. The temperature reading is taken whenever the patient happens to have an appointment. The majority of private patients are seen in the afternoon. Hospital patients are seen in the forenoon. I fail to note any difference in estimating the individual's family pattern.

PULSE, RESPIRATION AND BLOOD PRESSURE.

As clinical data is gathered while examining a red mucous membrane individual, the pulse rate is generally above 75 in the sitting position, the respiratory rate is usually above 18 in the sitting position, while the systolic blood pressure is usually above 125.

As clinical data is gathered while examining a pale mucous membrane individual, we generally find the pulse rate is usually below 75 in the sitting position, the respiratory rate is

usually below 18, while the blood pressure is usually below 125 systolic.

Having completed the examination of the patient, a decision is made as to the type of individual with which one is dealing. If a majority of the clinical data accumulated is above the accepted normal, the patient is classified as belonging to the plus family pattern. If a majority of the clinical data is below the accepted normal, the patient is classified as belonging to the minus family pattern.

Having classified the patient as belonging to either the plus or minus family pattern, I endeavor to prove whether the clinical observations, deductions and conclusions have been correctly made by outlining to the patient the family pattern syndrome he represents. Patients with seasonal hay fever as a rule belong to the minus family pattern.

THE MINUS FAMILY PATTERN SYNDROME.

In presenting the syndrome to the patient, one proceeds somewhat as follows: "My examination has been an effort to discover the family pattern you represent. I will describe the family pattern I feel you represent and when I have finished I wish you would let me know whether I am all wrong, 50 per cent correct, 75 per cent correct or better than 75 per cent."

In outlining this syndrome to the patient one cannot expect to be 100 per cent correct, because this syndrome is a composite one representing many individual syndromes gathered during the past 20 years. It is asking too much to expect all these many separate syndromes to be united in one single individual. Generally I am 75 per cent correct. About one-fourth of the time I am 90 per cent correct. If 50 per cent correct one can proceed with confidence in handling the patient. The minus family pattern syndrome is the one most often met in the practice of medicine. It is presented in the following manner:

The data gathered suggests that, from 15 to 25 years of age, you were very energetic. You could start the day's work early in the morning and continue until late at night without developing fatigue. If you were out late attending a party or

a dance, you would not feel tired the following day. Following the night's rest you would be refreshed, ready and willing to do a day's work again. Anyone trying to work with you and to follow you would wonder whether you never got tired and would find difficulty in doing an equal amount of work each day.

Later, as the years passed, there came a time when you found yourself tired at the end of the day's work, but a night's rest removed the sense of fatigue, enabling you to start the day fresh, only to be tired again at the end of the day. Still later, a night's rest did not remove the sense of fatigue and you found you started the day a bit tired. As time passed, you discovered you were more or less tired all the time, having developed a sense of fatigue that sleep did not remove. There ceased to be any pleasure in the day's work. You lost your drive and initiative somewhat, and began to feel that a fairly long vacation was necessary in order to feel well again.

Although you may tire physically, you never seem to tire mentally. If you sit down or lie down to rest, you pick up a newspaper, magazine, book or other work in order to be mentally employed. As a rule there is no lost mental time during the day. You are inclined to organize your life on a mental basis rather than a physical one.

IDEAL EXERCISE OF MINUS FAMILY PATTERN.

Exercise outside of the physical activity required for your daily work is disappointing because it is apt to leave you tired instead of refreshed in body and mind. The day following physical exercise you are apt to find that you are dulled mentally, being not nearly as alert.

The ideal exercise for one of your family pattern, if you feel the need of it, is gardening. The garden is never finished. It will hold your mental interest and satisfy your physical needs. What members of your family pattern need most is a mental house cleaning, which is best secured by having a hobby that does not require much physical activity. Music, stamp collecting, books, radio, cards, auto trips, camera, drawing, painting, crocheting, knitting, embroidering or one of the home crafts in wood or metal will bring an inner sat-

isfaction that will return you to your day's work refreshed in mind and body. Members of your family pattern are very susceptible to mental change. They often discover as the years pass by that if they are feeling tired and mentally depressed, an evening at the movie theatre, the reading of an interesting book, a short auto trip or time spent with an interesting hobby will leave them refreshed in mind and body as much as physical exercise refreshes members of the opposite family pattern.

THE SYMPTOM-COMPLEX.

When you feel right you sleep soundly. Another member of the family coming home late at night does not awaken you. You do not hear thunder at night or cars passing in the street. When you do not feel well you sleep lightly. It is easy for you to awaken between midnight and 3:00 A.M., but it is not easy to fall asleep again. Another member of the family coming home late at night awakens you. You hear thunder at night and cars passing in the street. You discover that you feel better at the end of the day than at the beginning. From 6:00 to 10:00 in the morning is more difficult for you to get through than from 6:00 to 10:00 in the evening. When bedtime arrives you are often wide-awake and at your best and are inclined to sit up, going to bed late.

You are apt to wake up in the morning with a mean feeling in the head, which generally wears off by the middle of the morning. If it does not wear off but becomes a real headache, that day is spoiled for you and you try to sidestep as much of the day's work as possible. You are apt to be troubled at times by a headache in the back part of your head, and a feeling of tightness in the back of your neck.

You are troubled at times by an itching head, which may be relieved by a shampoo. You are apt to be annoyed by an itching nose, which keeps you rubbing it frequently to allay the itching. Your skin is apt to itch. This itching may range all the way from an occasional scratching of the skin to the necessity of retiring when guests are being entertained in order to give your body a good scratching.

You are troubled by cold hands and feet. Your feet and hands go to sleep easily. If you cross your knees, one foot

soon goes to sleep. During the night it is not uncommon for one of your type to wake up with numb hands if you sleep with your arms crossed, making it necessary to rub the hands in order to restore feeling in them. You may possibly be annoyed by aching arms and legs at times. Occasionally you are troubled by cramps in your feet and legs which are relieved by a change in position or by standing on your feet.

You do not enjoy extremes of temperature. When it is 20° below zero here in the North during the winter months you do not care to go out-of-doors any more than is necessary. If you do go out, you generally plan to have your feet and hands dressed warmly in order to be comfortable. If your hands or feet become cold, you are usually very uncomfortable. On the other hand, when the thermometer during the summer months reaches 100° F. or more on certain days, you "flat tire" and have no ambition to work. You feel best when the temperature is either moderately warm or moderately cold. If you were obliged to choose between very hot weather and very cold weather, I expect you would choose the cold weather because you feel better in cold weather than very hot weather.

You do not enjoy extremes of temperature in your food. While some members of your family pattern enjoy hot foods, as a rule the majority like their food warm. It is not so satisfying when cold. If, in a restaurant, a plate of hot soup is placed before you, you are apt to wait for it to cool before eating it. While you can eat foods that come directly from the refrigerator to the table, as a rule you do not care for them. While you may eat ice cream, you do so slowly, taking longer than others to eat the same amount. You seem to want to warm it up in your mouth before swallowing it. While you drink ice water, you prefer to have the drinking water as it comes cold from the faucet.

You may be troubled by your ears blocking up at times. While you do not have many colds, when you do have one it is very apt to go down into your chest and last a long time. When you are tired, the resonance goes out of your voice.

When talking while tired, you discover you are obliged to put more effort into it in order for your voice to sound to you as it usually does. Those who know you well can tell

when you are tired by the lack of resonance in your voice. Your voice seems dull to them.

Members of your family pattern often believe they are inclined to be bilious because they have dizzy spells of short duration at times and there is often an uncomfortable sensation in the right side just above the waist line, which causes them to place their hand over the liver region frequently for a day or two.

For no reason that you can give you are apt to belch gas after eating. At other times a burning sensation in the stomach appears, coming on about an hour after eating. You occasionally have a feeling of abdominal distention so that you find it necessary to loosen your clothing around your waist line. Unless you have accustomed yourself to a regular time for the movement of your bowels daily, you probably are troubled by constipation. From time to time you are troubled with backache in the region of your waist line, which lasts from a few days to a week.

If the medical men you have consulted from time to time have been interested in operating, you have probably had one or more operations done. These are an operation on your nose, the removal of your tonsils, the removal of your appendix and an operation on your gall bladder.

All in all, you have good days and poor days, with the poor days representing the greater number. When you have a good day you feel wonderful and you wonder what ought to be done to feel well all the time.

As a rule members of the family pattern you represent live a long time. They generally live beyond 80 years of age. Probably in your family tree there are one or more individuals who lived to be 90 years of age or over.

DISTRIBUTION OF THE BLOOD MASS IN THE BODY.

Having estimated the racial pattern and the family pattern the individual represents, attention next turns to a study of the distribution of the blood mass in the patient's body.

We have in the body, as you already know, the peripheral vascular bed and the splanchnic vascular bed. The tissues supplied by the peripheral vascular bed include the skin,

muscles, bones, kidneys, brain, heart, lungs and upper respiratory tract. The tissues supplied by the splanchnic vascular bed include the liver, spleen, stomach and intestines. The blood lakes of the peripheral vascular bed are the skin and muscles. The blood lakes of the splanchnic vascular bed are the liver and spleen. The blood mass in the body rotates between the peripheral vascular bed and the splanchnic vascular bed. The appearance of a cold wave drains the blood from the peripheral vascular bed, transferring it to the splanchnic vascular bed. Ordinarily within a reasonable time, such as 24 hours represents, an adjustment of the blood mass takes place so that the peripheral vascular bed would again have its share. When food is taken in and digestion and absorption are necessary, the blood mass shifts to the splanchnic vascular bed. When the process of digestion is completed the blood mass shifts back to the peripheral vascular bed, there being a redistribution of the blood mass in the body according to tissue needs.

When the blood mass leaves the peripheral vascular bed the lumen of all the capillaries is lessened in size, which means less blood and, therefore, less hemoglobin with the oxygen it carries reaching the tissues. As a result of this lessened blood supply to the tissues, the tissues develop an oxygen want which we call anoxia.

In the developing of a clinical condition which results in the appearance of symptoms, a number of steps are visualized. The first step is the shifting of the blood mass from one or the other of the vascular beds. The second step which develops is an anoxemia in the capillary circulation of the vascular bed from which the blood mass has been drained.

The third step is the development of anoxia or oxygen-want in the tissues supplied. The fourth step is lessened cell-health or cell destruction due to tissue anoxia. The fifth step is the growth of micro-organisms in this tissue which is made suitable soil by the anoxia. The micro-organisms grow, multiply and destroy.

There are certain local symptoms associated with closure of a vascular bed. These include: *1.* altered nerve function expressed in pain; *2.* increased secretion of mucous membrane; *3.* edema of tissue; and *4.* ulceration of tissue. These

symptoms may be present in tissues supplied by the peripheral vascular bed or the splanchnic vascular bed, depending on which vascular bed is closed at the time. The length of time closure of a vascular bed continues determines whether one or all the above symptoms appear. The presence of these symptoms leads one to suspect the closure of a vascular bed.

PRESENCE OF OXYGEN-WANT IN TISSUES.

Oxygen, which is so essential to life, is normally obtained from the air by air-breathing animals. The air contains 20 per cent of oxygen. Complex mechanisms are involved in the intake and transfer of oxygen. These are sometimes interrupted, causing oxygen-want in the tissues.

Hemoglobin, the chief oxygen carrier of the blood, combines with oxygen of the air in the alveolar capillaries of the lungs. The oxyhemoglobin thus formed gives up oxygen to the tissues for their oxidation reactions. The rate and extent of all these reactions involving oxygen depend on the amount of oxygen available, in accordance with the basic law of mass action, which states that chemical action is proportional to the concentrations of each reacting substance.

In the lung venous blood is exposed to the alveolar gases which normally contain about 14 per cent of oxygen. Under these conditions, about 95 per cent of hemoglobin combines with oxygen to form oxyhemoglobin.

Anoxia, which is insufficient oxygenation of the tissues, may occur when the oxygen supply is diminished due to closure of one of the vascular beds.

PRIMARY SYMPTOMS OF ANOXIA OR OXYGEN-WANT IN THE PERIPHERAL VASCULAR BED.

1. A more or less constant feeling of fatigue in varying degrees which is not relieved by sleep.

2. Inability to sleep well at night.

3. Headaches of the migraine type.

4. Vertigo.

5. Inability to concentrate mentally. Difficulty in making business decisions. Has the butterfly type of mind, which flits from one subject to another.

6. There is a depressed mental state, with discouragement. A feeling that something is going to happen but does not know what it is.

7. Unexplained crying spells are present.

8. Twitching of muscles in various parts of the body, such as twitching of the eyelids and twitching of the corner of the mouth.

9. On account of the development of accommodation troubles while reading, the use of the eyes for close work is interfered with.

10. Double vision, especially when physically tired. This interferes with driving a car on long trips.

11. The speaking or singing voice tires easily, with loss of resonance.

12. There is shortness of breath of mild degree on moderate exertion.

13. Cramps or pains in muscles of the body most often used. This includes the muscles of the feet, calves of the legs, small of the back, upper and back part of the neck, and region of the heart on effort.

14. Neuritis-like pains in various parts of the body.

15. Tissue soreness in various parts of the body at different times. Patient, for example, will complain of soreness on swallowing, but on examination the throat appears to be negative. The soreness apparently is in the muscles used in the act of swallowing.

As a rule each individual does not have all the symptoms of this syndrome but has a majority of them. Quite frequently one finds an individual who has them all.

TREATMENT.

Treatment of patients with seasonal hay fever is divided into four divisions, in accordance with racial pattern, family pattern, vascular bed and oxygen-want requirements. In children, attention to the racial and family pattern requirements may be all that is necessary to render them symptom-free. In young adults of high school and college age the

meeting of racial and family pattern requirements plus a maintenance of an open peripheral vascular bed may render them symptom-free. In patients 40 years and older, in addition to attention to racial pattern, family pattern and vascular bed requirements, it is generally necessary to use three unit doses of a solution of zinc insulin crystals, given subcutaneously one or more times each week, in order to combat the edema of tissue and increased mucous membrane secretion, which are secondary manifestations of an oxygen-want existing in tissues supplied by the peripheral vascular bed.

In children, treatment may be started at the onset of symptoms. In young adults of high school and college age, treatment should be started two weeks before the expected onset of hay fever symptoms. In patients 40 years or over, treatment should be started six weeks before the expected onset of hay fever symptoms. Insulin in three unit doses is given once a week during the pre-onset period to these older patients.

RACIAL REQUIREMENTS IN TREATMENT.

When organizing treatment for a patient with seasonal hay fever the first thought is to reproduce in his food intake the same type of food that ancestors of the racial division he represents thrived on.

According to the draft maps of the World War, Vermont leads the country in the amount of hay fever and asthma. With very few exceptions patients I see with seasonal hay fever are Nordics. This means that in their daily food selection they should emphasize the protein and vegetable intake and keep low the intake of foods made from flour of any kind, cereals and all fruits. Their protein intake should be limited to sea food, fish, eggs, cheese, fowl and nuts. While they may eat all vegetables, they should place emphasis on green vegetables rather than red and yellow vegetables.

With many of these Nordic individuals, lettuce or raw cabbage is almost a daily necessity. When given the food their ancestors were accustomed to eat, these Nordic individuals will usually thrive, as does the cactus plant when given the environment its ancestors were accustomed to.

FAMILY PATTERN REQUIREMENTS IN TREATMENT.

The seasonal hay fever patients I see in Vermont are invariably members of the minus family pattern. The majority of the accumulated clinical data is below the accepted normal.

The minus family pattern individual has very definite requirements relating to his daily food intake. He handles wheat badly. White sugar is not for him, and muscle meats, such as beef, lamb and pork, are marked taboo. He must learn to do without milk as a beverage and omit citrus fruits from his daily food selection. Citrus fruit juices, such as lemon, grapefruit and pineapple, may be taken if diluted 75 per cent with water.

As a result he is asked to exchange foods made from white flour, whole wheat flour, graham flour and buckwheat flour for foods made from rye flour or corn meal. All wheat cereals should be exchanged for those which do not contain wheat.

He exchanges white sugar for honey. Muscle meats are exchanged for sea food, fish, eggs, fowl, nuts and meat from inside of the animal, such as liver, tongue, heart and kidney. Milk as a beverage, is exchanged for grape juice and water, equal parts. Nordic individuals apparently are unable to break down the curd formed in the stomach by milk within the time limit set by Mother Nature for the completion of the process of digestion. Citrus fruits and citrus fruit juices are exchanged for cranberry juice, apple juice and tomato juice. Nordic individuals do best when they have one or more tablespoons of some oil each day taken at meal time. Mazola oil, which is a cooking oil made from corn, is their favorite oil. Nordics need to grease their stomachs when eating protein food. As a rule Nordics are very fond of butter.

VASCULAR BED REQUIREMENTS.

Insofar as vascular bed requirements are concerned, efforts are directed towards maintaining an open peripheral vascular bed. To this end the patient is asked to add five drops of dilute hydrochloric acid and three drops of Amend's solution of iodine to a glass of water.

After stirring the contents of the glass, this mixture is swallowed. This is taken 20 minutes before breakfast and

20 minutes before the evening meal. If necessary, five drops of dilute hydrochloric acid in a glass of water are taken in the middle of the morning and the middle of the afternoon.

In prescribing Amend's solution of iodine, incense is burned to the patient's Nordic ancestors. Their sea food, fish, seaweed and sea moss intake guaranteed them a daily intake of iodine which enabled body metabolism to be carried on at a pace in keeping with their climatic environment. By prescribing Amend's solution of iodine, which is one-seventh as strong as Lugol's solution, an effort is made to duplicate the daily iodine intake which allowed the patient's Nordic ancestors to thrive in their environment.

Protein-eating animals have an acid saliva, while man has an alkaline saliva. Nordics down through the ages have been protein-eaters. Dilute hydrochloric acid 20 minutes before the morning and evening meal is an effort to imitate the acid saliva of animals who live on protein food.

Both the Amend's solution of iodine and dilute hydrochloric acid are given in an effort to allow the process of digestion and absorption to take place within the time limits set by Mother Nature. The iodine helps the thyroid to maintain its efficiency. By not delaying the process of digestion and absorption the blood mass is released from the splanchnic vascular bed and returns to the peripheral vascular bed, where it may nourish the tissues supplied by the peripheral vascular bed up to the time of the next intake of food.

OXYGEN-WANT REQUIREMENTS.

If the secondary symptoms of an oxygen-want in the tissues of the peripheral vascular bed are present, as evidenced by tissue edema, increased secretion of mucous membrane and possibly altered nerve function in the form of pain, then three units of solution of zinc insulin crystals are given subcutaneously in the arm one or more times a week. No effort is made to time the giving of the insulin. It is given at whatever time of day the patient has an appointment.

The severity of these symptoms governs the intervals at which the three unit doses of insulin are given. If very severe the insulin is given every other day. If moderately severe it is given on Mondays, Wednesdays and Fridays of

each week or at similar intervals. If less severe, then it is given on Tuesdays and Fridays.

As a maintenance dose it is given once a week until the hay fever season is over.

In giving insulin in three unit doses subcutaneously, one looks upon it as an oxidizing catalyst.

THE URINE REACTION AS THE PATIENT'S CONTROL.

Successful handling of a seasonal hay fever patient requires that the patient have a control that will enable him to estimate the status of the peripheral vascular bed in his body. The reaction of the urine, taken before meals with E. R. Squibb and Sons' nitrazine paper, serves as such a control. He endeavors to maintain an acid urine. His symptoms reappear or are made worse when his urine reaction shifts to the alkaline side.

Following the taking of food, the urine may shift to alkaline in accordance with what is called the alkaline tide in the body. A drop in weather temperature may shift the urine to alkaline. The alkaline tide follows the shifting of the blood mass to the stomach and intestinal tract to carry on the process of digestion and absorption. The drop in temperature with the coming of cooler weather closes the peripheral vascular bed.

When the urine shifts to alkaline the patient is asked to do two things. One is to take two teaspoonfuls of a honey, glycerine and lemon mixture before each meal until the urine reaction has returned to acid. This mixture is made by adding to an ordinary glass the juice of one lemon, two tablespoonfuls of glycerine and enough strained honey to fill the glass.

The second procedure is to drink liberally of cranberry juice during the day, either at meal time or between meals. This cranberry juice is made by pushing the contents of a can of cranberry sauce, which is really cranberry jelly, through a fine-meshed sieve, with the aid of a tablespoon, into a quart of cold water. Beat with an egg beater for a few minutes so that the water will dissolve all the cranberry jelly. Cranberries contain four acids, quinic, malic, citric and benzoic. They are considered a good source of iron, iodine and calcium.

In controlling his urine reaction the seasonal hay fever patient is taught to believe that an alkaline urine indicates a closed peripheral vascular bed, while an acid urine indicates an open peripheral vascular bed.

If one is interested in the study of allergy, then of necessity he must know thoroughly the contents of the several volumes written by Dr. William F. Petersen, of Chicago, on "The Patient and the Weather." At this time I wish to acknowledge the debt I owe Dr. Petersen for teaching me the importance in medicine of the peripheral and splanchnic vascular beds and the influence of the weather on the various biochemical processes in the patient's body. The day's first medical interest is the weather map and barometric pressure report received daily from Boston.

With scientific knowledge of the weather I know what I may expect at the hospital and in my office from patients in the way of symptoms and other clinical and laboratory data.

CASE REPORTS.

Case 1: J. M., age 5 years. During June, 1938, child first developed hay fever, which lasted two weeks. This year the eye and nose symptoms appeared at the same time during June, but this year the symptoms lasted six weeks. Mother wishes relief of child's symptoms.

Examination showed a blond-haired, blue-eyed, little Nordic girl with congested eyeballs and a running nose, standing with handkerchief in her hand ready to remove the watery discharge from her nose. Her father is Scotch and her mother English. Most of the people in the British Isles are Nordics. The mucous membrane in her nose was pale. Her temperature by mouth was 97.8°, and pulse 93. Because of her pale intranasal mucous membrane and subnormal temperature she was classified as belonging to the minus family pattern.

Her Nordic racial background suggests she is able to handle protein and vegetables but has difficulty with cereals and fruits. Her family pattern suggests she experiences difficulty in handling wheat, white sugar, muscle meats, raw milk and citrus fruits and citrus fruit juices. The first step in treatment is to learn what influence a change in food selection in accordance with her racial and family pattern needs will have on the closed peripheral vascular bed which is present.

A returned filled out diet history shows she has each week, 21 glasses of milk, six servings of muscle meat, a cereal each morning, seven oranges, two grapefruits, seven glasses of fruit juice, 20 slices of white bread, and candy and white sugar as desired.

She was asked to exchange foods made from white flour, whole wheat flour, graham flour and buckwheat flour for food made from rye flour and corn meal. All wheat cereals and all other cereals were to be omitted from the daily food selection in accordance with her racial background needs. The rye flour and corn meal foods were to be kept as low as possible in the diet. White sugar was exchanged for honey. Muscle

meats were exchanged for sea food, fish, eggs, cheese, fowl and nuts. Milk, as a beverage, was exchanged for grape juice and water, equal parts. All citrus fruits and citrus fruit juices were omitted. In other words, as the cactus plant does best when given the environment of its ancestors so, I feel, this little Nordic girl will do best when given an environment as near like that of her ancestors as possible. The following represents the clinical notes made since the first office visit on June 27, 1939:

June 30, 1939: Hay fever just the same.

July 5, 1939: Hay fever 50 per cent improved. Much less sneezing.

July 11, 1939: Since last visit has been symptom-free up to July 10, when went in swimming. Today sneezes, uses handkerchief and eyes are congested.

July 18, 1939: Since last visit has been perfectly well.

July 25, 1939: Has a five-minute sneezing period on rising each morning. Rest of day is symptom-free.

Aug. 1, 1939: Symptom-free except about one minute of sneezing on rising each morning.

Aug. 9, 1939: No more sneezing. For three days eyes were congested until after breakfast, when they appeared normal. Patient continued to remain symptom-free for rest of hay fever season.

Case 2: B. W., female, age 18 years. Seasonal hay fever appeared at 10 years of age. When 14 years of age, asthma began complicating hay fever. About June 1 each year eyes will begin to itch and sneezing attacks during the day will appear. Aug. 1, hay fever becomes severe and lasts until Oct. 1. The asthma is not constantly present but appears at intervals. When asthma appears is obliged to remain in bed. Ephedrine capsules relieve asthma in about 20 minutes. On skin testing reacts to blue grass, timothy, ragweed and house dust. The reaction produced by house dust exceeds the others. For past two years has had 16 injections each year in an effort to desensitize patient. The injections relieved the asthma phase but did not influence the nose and eye symptoms.

Examination showed a blond-haired, blue-eyed Nordic young woman. Her father is English and her mother Scotch. Her intranasal mucous membrane is pink in color. Temperature is 98.6°, pulse 74, respirations 15 and blood pressure 100/70. The majority of the accumulated clinical data being below the accepted normal, she was classified as a member of the minus family pattern. After presenting the minus family syndrome, she stated I was 90 per cent correct.

A food intake was advised in keeping with her racial and family pattern, as outlined in Case 1. A filled out diet history form showed she was having each week, 42 glasses of milk, 10 servings of muscle meat, seven oranges, two grapefruits, three glasses of fruit juice and 14 slices of white bread.

She was directed to add five drops of dilute hydrochloric acid and three drops of Amend's solution of iodine to a glass of water and, after stirring, to swallow such a mixture on rising in the morning and again 20 minutes before the evening meal. The dilute hydrochloric acid is an effort to imitate the acid saliva of animals who live on protein food. The Amend's solution of iodine is an effort to duplicate the daily iodine intake which the patient's Nordic ancestors derived from seaweed, sea food and fish. The patient was taught to use the urine reaction as a control and to keep the urine reaction on the acid side.

The following represent the progress notes made after the first office visit on June 29, 1939:

July 5, 1939: Eyes 100 per cent better than at first visit.

July 7, 1939: Eyes still normal. No sneezing spells yet. At this time of year usually has a sneezing spell each morning that lasts about three-fourths of an hour.

July 10, 1939: Eyes still normal. No sneezing spells.

July 12, 1939: Eyes still normal. One sneezing spell yesterday and today which lasted 10 minutes.

July 17, 1939: Eyes still normal. On July 13 and 15, sneezed more or less all day long. Urine reaction pH 7.5 on both these days. Lost sneezing spells when urine shifted to acid reaction. Much better than previous years at this time.

July 19, 1939: Eyes normal. No sneezing since previous visit.

July 21, 1939: Symptom-free since last visit.

July 24, 1939: Still symptom-free.

July 28, 1939: Symptom-free since last visit. During previous years at this date would be sneezing and have trouble with eyes all day long.

July 31, 1939: Still symptom-free.

Aug. 4, 1939: Symptom-free since last visit except on Aug. 2, when eyes and nose began to trouble. Urine reaction found to be pH 7.0. Drank liberal amounts of cranberry juice, which shifted urine reaction to acid. With shift of urine reaction to the acid side became symptom-free.

Aug. 7, 1939: Sneezed all the morning of Aug. 5, 1939. Urine reaction again pH 7.0. When shifted urine reaction to acid became symptom-free and has remained so. Ordinarily at this time in August would be sneezing all day. Eyes would itch and be congested. Nose would run water all day long. Eyelids would be so swollen they would almost be even with the cheek.

Aug. 14, 1939: On Aug. 11, 1939, woke up at 2:00 A.M. because of sneezing and watery discharge from nose which lasted until 9:00 A.M. The remainder of the day was symptom-free.

Aug. 17, 1939: Has been symptom-free since last visit. Has not had even a sneeze.

Aug. 21, 1939: Has been symptom-free since last visit.

Aug. 28, 1939: Has been symptom-free up to Aug. 27, 1939, when began to sneeze. Nose ran a stream of water and at times could not breathe through nose. Eyes did not trouble. Asthma did not appear. Today symptom-free again. Last visit gave three units of plain insulin to cure what patient was sure was a beginning head cold. Next day cold was all gone. Been able to sleep well each night.

Sept. 5, 1939: Has been symptom-free since last visit.

Sept. 12, 1939. Worked past two days in office which was cold because heat had not been started in building. As a result developed head cold. With head cold there has been no sneezing or other symptoms of hay fever. Insulin in three unit doses cured head cold after two treatments.

Case 3: Mrs. D. G., age 50 years. Fifteen years ago a load of hay came to a neighbor. Patient was asked to help neighbor's wife stow

away hay in hay loft. She immediately developed seasonal hay fever, and has had it each year since then. If, while riding in an automobile, she passes a field where haying is being carried on, her nose will block up and patient will sneeze. Hay fever starts the last week in May and lasts until frost appears. Hay fever is generally most severe during July. Most of the month of July is spent lying on the bed. Skin tests show a reaction to clover, timothy, ragweed, red top and house dust. One whole summer tried "injections for hay fever" but each one made patient sick. Patient's brother has seasonal hay fever.

Examination showed a gray-haired, brown-eyed, round-headed woman, five feet tall, weighing 111 pounds. Both her father and mother were Irish. Her intranasal mucous membrane was pale, temperature 98.2°, pulse 76, respiration 18, blood pressure 140/90. The color of the eyes and shape of head classify this patient as belonging to the Alpine division of the Caucasian race. This means that she is able to eat cereals and fruits, as well as proteins and vegetables. In outlining her food selection the object would be to remove from her food intake white flour, white sugar and other refined foods. She was asked to exchange wheat foods for rye or corn meal. White sugar was exchanged for honey. Milk, as a beverage, was exchanged for grape juice and water, equal parts, in order to avoid the curd formation following the drinking of milk. Citrus fruits and citrus fruit juices were omitted. Five drops of dilute hydrochloric acid and three drops of Amend's solution of iodine in a glass of water were prescribed to be taken on rising in the morning and twenty minutes before the evening meal. Five drops of dilute hydrochloric acid were taken at 10:00 A.M. and 3:00 P.M. Three units of zinc insulin crystals were given subcutaneously in the arm on Tuesdays, Thursdays and Saturdays. Later, when symptoms improved, the insulin was given on Tuesdays and Fridays, each week.

The following represent the progress notes since first visit on May 29, 1939:

June 1, 1939: Hay fever has not yet appeared.

June 4, 1939: No hay fever yet.

June 7, 1939: No hay fever.

June 15, 1939: Hay fever generally starts at Memorial Day time, but this year no hay fever until June 15, 1939: Can always plan on hay fever starting May 30 so feels that for the first time hay fever appearance has been delayed two weeks this year. Today hay fever present nearly all the forenoon. Sneezed all the morning. Nose blocked up, watery discharge from nose, eyelids itched. Since noontime no hay fever.

June 22, 1939: Nose been worse past three days. Last year would sneeze all day long. Nose would run water and block up. This year so far is 50 per cent better than last year; is not having long sneezing spells. This year by 10:30 A.M. each day will be free from sneezing and nose will open up. Will remain so until about 5:00 P.M. Then at 5:00 P.M. will have sneezing and watery discharge from nose lasting about two hours. Sleeps well at night.

June 24, 1939: Condition same as at previous visit.

June 27, 1939: Had a bad day on June 25, 1939, but since then has been much better.

June 29, 1939: Patient states that on days she is given three units of insulin she will be symptom-free from symptoms during the remainder of the day. Hay fever symptoms during the month of June this year are 50 per cent better than previous years. Does not have hay fever symptoms more than half a day, instead of all day as in previous years.

July 1, 1939: On days I give patient three units of a solution of zinc insulin crystals at 2:30 P.M., she observes the following: 1. Nose stops running water for the rest of the day. 2. Sneezing stops. 3. Nose 50 per cent more open for rest of the day. 4. Feels much more like working the rest of the day. Yesterday had a very good day. Today has not been too bad.

July 3, 1939: Been very good since last visit; 90 per cent better.

July 6, 1939: Was symptom-free until July 5, there being no hay fever symptoms until bedtime, when nose blocked, ran water and patient sneezed. Sat up from 1:00 A.M. to 3:00 A.M. The rest of the night slept well. Generally at this time of year spends most of time lying on bed during the day. Now, if lies down 15 minutes feels rested and ready to do housework again.

July 10, 1939: Was very good, July 7 and 8. July 9, nose ran water and eyes itched.

July 13, 1939: Insulin given on July 10 cleared up nose for rest of the day. July this year is 75 per cent better than any previous July since hay fever started. Is able to sleep well nights.

July 18, 1939: Since last visit has sneezed some each day.

July 20, 1939: Been symptom-free.

July 25, 1939: Symptom-free.

July 27, 1939: Symptom-free.

Aug. 1, 1939: Patient states she had a very comfortable month of July. Began at this date giving three units of insulin on Tuesday and Friday instead of three times a week.

Aug. 4, 1939: Symptom-free.

Aug. 8, 1939: Symptom-free.

Aug. 19, 1939: Still symptom-free.

Aug. 26, 1939: No sneezing until this morning. Sneezed four or five times. Nose remains open.

Sept. 2, 1939: With exception of one day has been symptom-free since last visit. Has not lost a whole night's rest this hay fever season. With the exception of one night has slept well each night.

Sept. 9, 1939: Symptom-free since last visit.

Sept. 16, 1939: Symptom-free since last visit.

SUMMARY.

1. The object in examining the seasonal hay fever patient is to determine his racial pattern, his family pattern, the status of the peripheral and splanchnic vascular beds and the presence of an oxygen-want in the tissues supplied by the peripheral vascular bed.

2. In determining the patient's racial pattern one decides whether he is a member of the Nordic, Alpine or Mediterranean division of the Caucasian race.

3. In determining the family pattern one decides whether the patient represents the minus family pattern, in which the majority of the clinical data is below the accepted normal.

4. In determining the status of the peripheral and splanchnic vascular beds one studies the color of the mucous membrane in the nose.

5. In determining the presence or absence of oxygen-want one estimates whether the primary and secondary symptoms of oxygen-want are present.

6. The food commonly used by the racial division the patient presents is prescribed.

7. The food selection adapted to the minus family pattern is prescribed.

8. Dilute hydrochloric acid and Amend's solution of iodine are both taken in the same glass of water 20 minutes before the morning and evening meals.

9. Three units of a solution of zinc insulin crystals are given subcutaneously in the arm one or more times a week to serve as an oxidizing catalyst.

10. Under the above regimen it is possible to control the symptoms during the hay fever season.

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THE AMERICAN LARYNGOLOGICAL, RHINOLOGICAL AND OTOLOGICAL SOCIETY, INC.

The Forty-sixth Annual Meeting of the Society was held at the Waldorf-Astoria Hotel in New York, June 6, 7 and 8, 1940. There were 212 members and 81 guests in attendance, a total of 293. The 212 members included 21 of the 25 candidates elected at this meeting; the 81 guests included 17 applicants for membership. This was the largest meeting ever held by the Society.

NEW YORK ACADEMY OF MEDICINE.

SECTION ON OTOLARYNGOLOGY.

Meeting of Dec. 20, 1939.

Pharyngomaxillary Fossa Infection. Dr. Raymond J. Gaffney (by invitation).

(To be published in a subsequent issue of THE LARYNGOSCOPE.*)*

The Use of Colloidal Thorium Dioxide in Roentgenography of Paranasal Sinuses. Dr. Russell C. Grove.

(To be published in a subsequent issue of THE LARYNGOSCOPE.*)*

Meningitis and Temporal Bone Abscess Secondary to Suppurated Petrositis. Clinical Course with Sulfanilamide. Dr. Eugene R. Snyder.

(To be published in a subsequent issue of THE LARYNGOSCOPE.*)*

Cerebrospinal Rhinorrhea. Pathological Findings. Dr. Max L. Som and Dr. Rudolph Kramer.

(To be published in a subsequent issue of THE LARYNGOSCOPE.*)*

Polypoid Tumors of the Esophagus. Dr. John J. Mahoney (by invitation).

(To be published in a subsequent issue of THE LARYNGOSCOPE.*)*

Two Cases of Esophageal Foreign Body with Complications. Dr. F. Vistreich.

(To be published in a subsequent issue of THE LARYNGOSCOPE.*)*

Osteogenic Fibrosarcoma of the Temporal Bone. Dr. Harold W. Corya.

(To be published in a subsequent issue of THE LARYNGOSCOPE.*)*

Sphenotemporal Lobe Abscess with an Analysis of Little Known Symptoms. Dr. David L. Poe (by invitation).

(To be published in a subsequent issue of THE LARYNGOSCOPE.*)*

(Continued from June issue.)

DISCUSSION.

DR. JACOB L. MAYBAUM (Dr. Eugene Snyder's case): This patient was one of six cases of otitic meningitis under our care at Mt. Sinai Hospital last winter and the winter before. We were enabled during that period to observe the variation in the clinical picture with the use of sulfanilamide under different conditions. Of these six cases, five due to streptococcus hemolyticus recovered, and one due to pneumococcus type III died. In the latter, the clinical course under sulfapyridine was much prolonged. In the treatment of these patients we observed that a considerable reduction in the dose of sulfanilamide during the active course of the disease resulted invariably in a flare-up of

symptoms; furthermore, inadequate dosage simply prolonged the course. We observed that, in addition to the influence of inadequate dosage, incomplete drainage for one reason or another resulted in a picture of a chronic meningitis, lasting for two months, as in the instance of the patient reported by Dr. Snyder. There were times when the findings on spinal fluid examination gave the only evidence of the presence of a bacterial meningitis, the patient being symptom-free during such periods.

Two factors must be considered: 1. Maximum doses should be given in the early stages of the disease and maintained with reduced doses over a long period. 2. As far as possible, adequate surgery should be employed. When a patient with an otitic meningitis, who is receiving large doses of sulfanilamide so that the blood level content is 12 or 15 mg. per 10 cc. of blood, persistently on spinal fluid examination still gives evidence of a meningitis, we may assume that the focus of infection has not been sufficiently dealt with.

We were forcibly impressed, in the early days of the use of sulfanilamide for meningitis, by a case report of Smith and Coon in the January number of the *Archives of Otolaryngology*. I have referred to that case on a number of occasions. The patient had received sulfanilamide for an upper respiratory infection with a middle ear infection. Following a mastoidectomy, the patient ran a septic temperature, which aroused the suspicion of the presence of a sinus thrombosis; the blood cultures were repeatedly negative. It occurred to someone that it might be a good plan to do a Tobey-Ayer test. A cloudy spinal fluid with a high cell count and a positive culture for streptococcus hemolyticus was discovered on examination. The patient had throughout run a symptom-free, euphoric course. The mastoid wound was revised and large doses of sulfanilamide were given, followed by recovery.

One other point, and that is that sulfanilamide should be given as a preliminary treatment for 24 or 48 hours in severe cases of otitic meningitis. It is far better not to operate upon such patients before this time, but to saturate them thoroughly with the drug and use whatever supportive measures we can. We have followed this procedure with better results as far as the patient was concerned. One of our cases was a child with double mastoid, in extremis, with all evidences of profound shock and overwhelming meningitis. We gave the child large doses of sulfanilamide for 24 hours, and the clinical picture changed much for the better. At the end of that time I did a double mastoidectomy and the clinical course was quite satisfactory.

Dr. David L. Poe: I would like to ask what size doses of sulfanilamide were used, and how old was the child?

Dr. Jacob L. Maybaum: Of our cases of streptococcus meningitis which have recovered under operation and sulfanilamide therapy, one was a child, age 7 years. We gave this child as high as 250 to 270 gr. of sulfanilamide daily. The important point is not so much the size of the dose but the maintenance of a content of 10 to 12 mg. of sulfanilamide per 100 cc. of blood. Some are inclined to ignore this method of gauging the dose, but I believe the dosage is better controlled in that than in any other manner. The dose has been empirically set at 15 gr. to 20 pounds of body weight, but this dose should not be adhered to too closely. The point, in the serious condition with which we are dealing, is to saturate the patient so as to get a high blood level as quickly as possible.

(To be continued in a succeeding issue.)

BOOK REVIEW.

The Mechanism of the Human Voice. By Robert Curry, M.A., Ph.D. (Dunelm); formerly Demonstrator in Psychology, Edinburgh University, etc. With Foreword by Douglas Guthrie, M.D., F.R.C.S., F.R.S., Edin., Consulting Aural Surgeon, Royal Hospital for Sick Children, Edinburgh. With 20 illustrations. New York: Longmans, Green and Co. 1940. Price $3.00.

This monograph is presented for the purpose of clarifying and correlating many diversified lines of study upon the human voice. Perhaps no contemporary student of the subject is better fitted to present such a work, and with such a purpose in mind, than Mr. Robert Curry. This will at once be obvious to all who study this outstanding contribution. As Douglas Guthrie points out in the Foreword, Robert Curry has in succession devoted himself to English, Education, Physics, Phonetics, Psychology, Anatomy, Physiology and Laryngoloy, and his book throughout its pages reflects this comprehensive training which makes it possible. While the author insists that his book is intended merely to serve as a guide to further study, it, nevertheless, presents each of many phases in sufficient detail to satisfy all who would have a rather broad glimpse into practically every branch of the subject. For those who seek to make a special study of one phase or another, the author has made available an exhaustive bibliography of 400 references. There is in addition an adequate index.

Following a brief general description of the nature and development of the voice and resumé of definition of terms pertaining thereto, the opening chapters are devoted to a description of the anatomy of the vocal organs, including the mouth and pharynx, the larynx, neck, thorax and abdomen, insofar as they pertain to the subject in hand. There is included a fine description of the nerve supply particularly to the larynx. The anatomical resumé is brief but adequate, and provides a good review for those relatively familiar with the subject. At the same time students who are not primarily anatomists or laryngologists will find the anatomical descriptions entirely sufficient to enable them to understand the remainder of the text. A chapter dealing with the difficult subject of acoustical problems of voice, including physical principles concerned in the production of sound waves in general, and resonance, as well as the physics involved in the action of the larynx as a sound producing organ, is for the most part understandable by the non-physicist. The description of the "Physiology of Phonation" includes a discussion of the action of the laryngeal muscles and their effect upon the vocal cords and allied structures, and points out how variations in the activity of each control such facts as duration, pitch, intensity and quality of the sound produced.

Passing to a consideration of the "Mechanism of Speech," the author discusses classification and such phenomena as intonation, articulation and articulatory movements, including the production of vowels and consonants. A chapter devoted to the singing voice includes a discussion of the physiology and mechanics of the vibrato, tremolo, falsetto and nasality and, in addition, a summary of singing technique, vocal training, and a description of vocal disorders resulting chiefly from improper use of the vocal organs.

The anatomy of the ear, together with a resumé of the mechanism of normal sound perception and deafness, leads to a discussion of the interrelationship between normal and impaired hearing, and speech.

Chapters on the "Experimental Study of Voice" describe, in brief, methods utilized in studying the physical properties of sound as produced by the larynx, and the more commonly employed methods of experimentally and clinically studying the physiology of voice production and the action of the

larynx. These are given passing attention, with no attempt to include more than a resumé of the subject. It does, however, give an excellent insight into the technical methods available for the study of the problem, cites a few outstanding observations made by each method of approach and evaluates the importance and scope of the various techniques.

Concluding chapters on disorders of speech and voice contain a brief discussion of stammering, stuttering and certain organic defects, including psychological and neurological disorders and the psychoses. The final chapter is a most interesting consideration of the voice as affected by personality.

It must be expected that in so comprehensive and yet brief treatise covering the subject from the standpoint of a great variety of scientific viewpoints difficulty will be found in following some of the more highly technical passages and with an understanding of the terminology. The book is, therefore, primarily for the more advanced student. Likewise, it is necessary to realize that, in order to keep the book within bounds, many phases must be covered rather sketchily. It perhaps will serve its best purpose in calling attention to newer trends and in presenting students of one phase of the subject with a working knowledge of various other aspects of the study of voice production. From this standpoint the text is all-inclusive and probably has no equal.

"The Mechanism of the Human Voice" is especially well written, its approach is highly scientific and bears in every line the unmistakable stamp of authority. Nothing since Negus' monumental "Mechanism of the Larynx" will have served as so authoritative a source of reference as this book by Curry. It is to be hoped, however, that future editions may find this brilliant text considerably enlarged, more profusely illustrated and the rather poor anatomical drawings improved in quality.

This book richly deserves to be included in the library of everyone interested in any phase of the production of the human voice. J. J. P.

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